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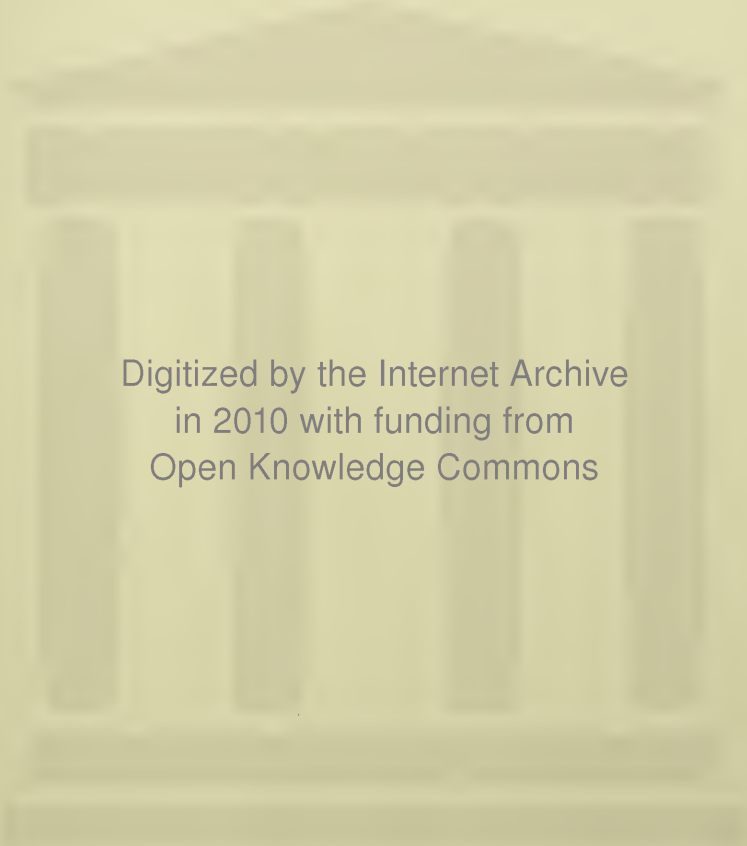
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THE BLOOD
AND ITS
DISEASES.

HENRY IRVING BERGER, M. D.

1915.

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CHAPTER I.

DISEASES OF THE BLOOD

1. SIMPLE OR SECONDARY ANEMIA

DEFINITION:

Anemia denotes an insufficiency in the amount of blood especially in the number of red cells and in the percentage hemoglobin.

The causes of all secondary anemias are known.

The most frequent cause is hemorrhage.

In simple anemia, regeneration of blood occurs in a normal manner.

CLASSIFICATION AND ETIOLOGY:

1. **Surgical Hemorrhage.** (Operations.)
2. **Traumatic Hemorrhage.**
 - (a) External or visible hemorrhage.
 - (b) Internal or concealed hemorrhage.
3. **Pathological conditions** and other causes
 - (a) Hemorrhages from **genito-urinary tract.**
 - (x) Hematuria. (See p. 106.)
 - (y) Menorrhagia. (See p. 114.)
 - (z) Metrorrhagia. (See p. 114.)
 - (b) Hemorrhage from **gastro-intestinal tract.**
 - (y) Hematemesis. (See p. 100.)
 - (z) Melœna. (See p. 119.)
 - (c) Hemorrhage from **respiratory tract.**
 - (y) Hemoptysis. (See p. 104.)
 - (z) Epistaxis. (See p. 118.)
 - (d) Hemorrhagic diathesis.
 - (e) Infectious diseases.
 - (f) Diseases associated with **albuminuria.**
 - (z) Acute and chronic Bright's disease.
 - (g) Chronic **suppurative diseases.**

(h) **Toxic Conditions:**

(y) Mineral poisoning especially lead.

(z) Acute rheumatic fever.

(i) **Parasites:**

(x) Malarial.

(y) *Bothriocephalus latus*.

(x) *Anchylostoma*.

(j) Bad hygienic conditions and improper food.

DIAGNOSIS: The typical blood-picture is:

1. Reduction in percentage hemoglobin (**oligochromemia**) and a corresponding decrease in the number of red cells (**oligocythemia**). These deviations as a rule run parallel.
2. Changes in the erythrocytes:
 - (a) **Poikilocytosis** is slight. The more severe the anemia the more marked is the alteration in size and shape of the R. B. C.
 - (b) **Polychromatophilic degeneration**. Varies greatly, but is best marked after hemorrhage.
 - (c) Nucleated red cells (**normoblasts**). Microblasts also found especially in connection with malignant tumors of the intestinal tract.
3. Absence of leucocytosis. But after hemorrhage a "relative leucocytosis" occurs.
4. **Eosinophilia**, if anemia be due to parasites.

SYMPTOMATOLOGY of Hemorrhagic Anemia:

1. **General Remarks:**

Anemia varies with rapidity of the blood lost and individual peculiarity of the patient. Bleeders recuperate quickly. Women stand the loss of blood better than men. If one-half the total volume of blood be lost death will ensue.

2. **Pallor**. The more blood lost the greater the whitening of the skin and mucus membranes of the eyes and lips.
3. **Dyspnea**. Respirations increased.
4. Sweating and corresponding thirst.
5. **Vertigo** and nausea.

6. **Shock and collapse** in proportion to amount of blood lost. The same symptoms occur in concealed as in external hemorrhage.

7. **Circulatory symptoms.**

Pulse: Weak at first due to loss of volume of blood which is necessary for the heart to work with. Saline infusions restore this necessary volume. If patient becomes exsanguinated the pulse becomes imperceptible.

Functional murmurs:

(a) **Hemic:** are systolic in time, untransmitted and heard best over base.

(b) **Continuous venous hum** (bruit au diable). By pressure over jugular vein it may be made to disappear.

Note: When the anemia improves these murmurs disappear.

8. **Amenorrhea.** In chronic cases in women there may be a suppression of menses.

2. PROGRESSIVE PERNICIOUS ANEMIA. (Addison's Anemia—Biermer's Disease.)

DEFINITION.

An "idiopathic" anemia growing progressively worse characterized by abnormal regeneration of the blood and by hemolysis.

It usually occurs after the age of 36.

Although the *Bothriocephalus Latus* may cause such an anemia it is amenable to treatment.

DIAGNOSIS. "It is a large cell anemia."

(A) BLOOD PICTURE.

Changes in the red cells.

(a) **Normoblasts and megaloblasts.**

As a rule the megaloblasts out-number the normoblasts.

"Crises" of either of these forms may occur.

(b) **Poikilocytosis** very exaggerated.

(c) **Polychromatophilic degeneration** extensive.

- (d) **Oligocythemia.** The absolute count of both R. B. C. and W. B. C. is reduced from 20 to 50%.

Leucopenia. The reduction in the white count runs parallel with the reds.

Hemoglobin relatively increased. Color index is therefore high since the R. B. C. are decreased.

(B) **SYMPTOMS.** The disease develops insidiously with:

1. Progressive general weakness without noticeable emaciation.
2. Gradually increasing profound anemia. Lemon-yellow, puffy face associated with an increase in weight is very characteristic.
3. Pronounced cardiac enfeeblement, dyspnea, vertigo, palpitation, breathlessness on exertion very marked. Hemic murmurs may occur even without valvular lesions. Advanced cases may end up with fatty degeneration.
4. **Digestive disturbances** with periodical attacks of **diarrhea** occur in 50%.

Nausea and vomiting very frequent.

Diarrhea may be associated with paroxysmal pains in the stomach.

Depraved appetite and yet the patient lays on weight and flesh.

5. Slight **edema** of the subcutaneous tissues.

Usually first perceptible about the ankles and feet.

6. Involvement of the spinal cord causes:

Tingling and numbness of the extremities.
Neuritic pains at times.

Some show features of lateral sclerosis with spastic features and increased reflexes, while

Others resemble tabes: lightning pains, girdle sensation, areas of anesthesia, loss of reflexes.

7. Subcutaneous hemorrhages in the form of petechia are not as common as **retinal hemorrhages**.
8. Fever. Slight and variable.
9. Periods of remittency. But the symptoms soon return.

3. CHLOROSIS.

DEFINITION.

A primary anemia without cachexia, occurring exclusively in young girls and in young women, characterized by a greenish coloration of the skin and a great reduction in hemoglobin.

DIAGNOSIS. Confirmed by a blood examination.

1. Hemoglobin tremendously lowered.
2. Changes in red cells:
 - (a) Pessary or ring-shaped cells predominate. They are called "dropsical cells."
 - (b) Macrocytes and some microcytes but no nucleated cells.
 - (c) Polychromatophilic degeneration.
 - (d) Poikilocytosis in severe cases only.
 - (e) Total blood count normal or perhaps slightly below. Usually about 4,000,000. Color index is therefore low.
3. No change in leucocytes.
4. Blood plates increased in number.
5. Blood plasma increased. Normally the corpuscular and plasma elements of the blood are equal in volume. In chlorosis the plasma is raised to 75% and the corpuscular volume reduced to 25%.
6. Specific gravity reduced. May be as low as 1030.

SYMPTOMS.

1. Pallor. Face varies in color from a pale yellow to a greenish hue. The swelling under the eyes gives the patient a "nephritic" appearance.
2. Stomach symptoms.
 - (a) Depraved and perverted appetite.
 - (b) Hyperacidity with or without gastric ulcer.
 - (c) Obstinate constipation.
3. Neuralgias:
 - (a) Occipital and supraorbital.
 - (b) Gastralgia and intercostal neuralgia.
4. Amenorrhea.
5. Palpitation very prominent in many cases.

PHYSICAL SIGNS.

1. **Tissues pit on pressure** (edematous infiltration).
2. **Systolic functional murmurs** which disappear as soon as the disease is cured. Murmur is heard best over pulmonary artery but is not transmitted, and second pulmonic sound is not accentuated.

The bruit-au-diable is heard over the sterno-clavicular articulation.

Rapid heart and rapid pulse. The heart may ultimately enlarge.

4. LEUKEMIA.

DEFINITION.

A progressive, chronic and permanent disease of the blood and hematopoietic organs (marrow, spleen and lymph glands) especially those concerned in the genesis of the white corpuscles which are found to be enormously increased in number.

The leucocytosis here is permanent whereas in other diseases it is more or less transitory.

VARIETIES.

- (A) Spleno-medullary leukemia ("myelemlia").
- (B) Lymphatic leukemia ("lymphemia").

SPLENO-MEDULLARY LEUKEMIA. BLOOD PICTURE.

1. **Changes in the white cells.** Tremendous increase in the absolute count. Average is 350,000 per c.mm.

The differential count is (according to Webster):

- (a) **Neutrophilic myelocytes.** These average 35% of the total white count. These cells are large mononuclear cells with neutrophilic granules. They appear in two forms:

1. **Large myelocyte of Cornil.** Has a large, pale eccentric nucleus which is poor in chromatin. These cells are only diagnostic of this disease.
2. **Small myelocyte.** Is about the size of a normal polynuclear leucocyte, has a centric round nucleus staining deeply with the various aniline dyes.

Note.—All gradations are seen between these two types.

- (b) **Polynuclear neutrophile leucocytes.** These are "relatively" decreased in number. The absolute count is increased. 60,000 to 75,000 of these cells may be present. They average 46% of the total white count.

These cells vary greatly in size: something never seen in ordinary leucocytoses.

They are frequently degenerated, their nuclei being pale and showing karyokinesis.

- (c) **Eosinophiles.** Usually increased but their percentage relation to the other white cells is unaltered. Average is 5%. They vary greatly in size.
- (d) **Basophiles.** The mast cells are increased, the absolute count in some cases being greater than that of the eosinophiles and always proportionately higher.
- (e) **Lymphocytes.** As a rule the percentage is reduced to an average of 10%. The absolute count is however increased. Large cells predominate over the small cells and in both forms degenerative changes are frequent.

2. Changes in the red cells.

- (a) **Oligocythemia.** The absolute count is decreased from 10 to 40%. The cells approach the chlorotic type.

- (b) **Nucleated reds** are numerous.

Normoblasts only.

If megaloblasts and giantoblasts be present the prognosis is bad.

The larger nucleated red cells never exceed the normoblasts in number.

- (c) **Polychromatophilia** is more or less common. Many cells show **basophilic granulations**.

The following equations will elucidate the diagnosis:

(a) in health: W.B.C.: R.B.C.: 7,000:4,500,000

(b) in leukemia: W.B.C.: R.B.C.: 350,000:3,500,000.

A ratio of 1:650 in the first case as compared to 1:10 in the latter.

3. **Hemoglobin reduced.** Average is 40%.
4. **Color index is low.** Average is 0.6.
5. **Low specific gravity.** The blood is pale and sticky.

SYMPTOMS OF SPLENO-MYELOGENOUS LEUKEMIA.

Onset. General malaise, weakness, pallor, some emaciation and digestive disturbances.

1. Progressive **dyspnea** due to progressive increase in size of the spleen.
2. **Early enlargement of the spleen.** It is usually painful and progressive.
3. Those symptoms due to splenomegaly itself.
 - (a) Ascitic accumulations in abdomen.
 - (b) Dropsical infiltration of extremities.
 - (c) Recurrent hematemesis.
4. Hemorrhages into the skin and mucous membranes may follow the appearance of the splenic tumor.

Bleeding from the nose is very common.

A hemorrhage or a free diarrhea may reduce the size of the spleen.

5. The lymph glands may also enlarge after the spleen has enlarged but not always.
6. Gastro-intestinal disorders.
7. Obstinate priapism very frequent.
8. Defective hearing and vision. (Leukemic retinitis).
9. Febrile and afebrile periods common.
10. The liver may also become enlarged.

LYMPHATIC LEUKEMIA. BLOOD PICTURE.

1. An absolute leucocytosis with a preponderance of **lymphocytes**. Average leucocyte count is 145,000.
2. In contrast to the spleno-myelogenous form in which the granular cells are increased, we find here an increase in the **nongranular mononuclear** cells.
3. Both large and small lymphocytes are present depending upon the stage of the disease.
4. These leucocytes show degeneration of both protoplasm and nuclei but only few cells show mitosis which is so common in the other form of leukemia.
5. The lymphocytes constitute about 95% of the total white count, the polymorphonuclear cells therefore being insignificant in number.
6. Anemia is of a severer grade than in the other form. The average hemoglobin percentage is 37.
7. In exceedingly grave cases only, do we find nucleated red cells.

SYMPTOMS IN LYMPHATIC LEUKEMIA.

(A) **ACUTE LYMPHATIC LEUKEMIA.** (Young people usually affected.)

1. Hemorrhages into the skin.
2. Rapidly developing cachexia and anemia.
3. Angina. (Usually of the ulcerative type.)
4. Swelling of the glands. Usually cervical.
5. Fever. 103° to 105° .

(B) **CHRONIC LYMPHATIC LEUKEMIA.**

1. Occurs later in life.
2. Gradual, progressive and painless enlargement of the lymph glands usually first affecting the glands of the neck, then the axillary and in time become generalized.
3. Spleen and liver may also be enlarged.
4. Anemia approaches gradually.
5. Hemorrhage and fever are rare.
6. Pruritus may be very intense.
7. Bones are very tender.
8. Metabolism practically unchanged.
9. Small lymphocytes predominate.

5. HODGKIN'S DISEASE.

DEFINITION.

A disease of the lymphatic structures having the following characteristics:

1. **Cervical glands enlarged.**

- (a) The glands of the neck are first to enlarge (sometimes one at the angle of the jaw.)
- (b) Only one side at first involved.
- (c) From this point all the other glands are involved progressively downward, i. e., axilla, elbow, groin, etc.

Characteristics of these glandular enlargements:

- (a) Progressive increase in size.
- (b) Painless throughout the disease.
- (c) First soft, later becoming hard.
- (d) Discrete: each gland can be mapped out from the adjacent gland.
- (e) Freely movable under the skin.

2. **Splenomegaly** not as marled as in leukemia.

3. Those features of a **secondary anemia**.

Red cells usually between 3 and 4 million. But, the more pronounced the cachexia the greater the oligocythemia.

White cells normal or perhaps slightly increased. Average is about 10,000.

Exaggerated leucocytosis of leukemia is absent. A relative lymphocytosis is diagnostic.

May be diagnosed from spleno-medullary leukemia by the fact that in Hodgkin's disease the relation of lymphocytes to polynuclear cells is 3 to 1 instead of normal, 1 to 3.

Those cases in which the leucocytes are increased the prognosis is unfavorable.

Hemoglobin reduced in proportion to R. B. C.

4. **Pressure symptoms.**

- | | |
|------------------|------------------------------|
| (a) Dyspnea. | (d) Ascites. |
| (b) Hydrothorax. | (e) Swelling of extremities. |
| (c) Dysphagia. | (f) Jaundice. |

DIFFERENTIAL DIAGNOSIS.

HODGKIN'S DISEASE.

Lymphatic hyperplasia is general but the cervical glands are the starting point.

It is first unilateral and subsequently involves the other side.

The glands grow rapidly but always remain discrete.

The glands are first soft and elastic, later becoming hard.

TUBERCULAR CERVICAL ADENITIS.

A localized disease, the cervical glands are more often tubercular than any other glands of the body. It is never generalized.

Bilateral from the start but more marked on one side than on the other.

The rule is that the glandular "kernels" become matted together.

At first hard and the skin is freely movable over the kernels. Later, the glands soften and suppurate. When suppuration ensues the glands become adherent to the skin,

DIFFERENTIAL DIAGNOSIS—Continued.

HODGKIN'S DISEASE.	TUBERCULAR CERVICAL ADENITIS
Not only are the lymph nodes affected but also the spleen. Large nodular growths are found in this organ, in the liver, etc. This internal lymphatic hyperplasia causes various pressure symptoms: ascites, jaundice, dyspnea, etc., according to location. An excised portion of a gland shows lymphoid structure.	and discharging fistulæ may form. Lymph glands only affected. Tubercle structure.

Note—Both diseases are common in children and in both may the tuberculin reaction be obtained. It is, however, obtained only in advanced cases of Hodgkin's disease when the cachexia is very marked.

6. SPLENIC ANEMIA—BANTI'S DISEASE.

DEFINITION.

A special form of anemia, chronic in nature, associated with enlargement of the spleen (splenomegaly) but without palpable lymphatic glandular hyperplasia and by occurring by preference in children.

DIAGNOSIS.

1. Tendency to hemorrhage, especially epistaxis.
2. Enlargement of the spleen associated with secondary enlargement of the liver due to cirrhosis. The texture of the spleen is hard and it increases with the progress of the disease. Splenomegaly is never as great as in spleno-medullary leukemia.
3. Jaundice and pigmentation of the skin.
4. Blood picture:

Very variable, though, in many respects, it resembles that of secondary anemia, i. e., R. B. C. and Hb. reduced in same proportion and low color index.

Usually slight reduction in absolute W. B. C. Relative lymphocytosis (Webster). Relative decrease in polynuclears.

BLOOD CHART.

	HEMOGLOBIN	ABSOLUTE WHITE COUNT	ABSOLUTE RED COUNT	ABNORMAL REDS	ABNORMAL WHITES
SECONDARY ANEMIA.	Correspondingly reduced. Oligo- chromemia. Low color index.	Unaltered. Re- lative leucocyto- sis after hemor- rhage.	Reduced in pro- portion to sever- ity of hemor- rhage (Oligocy- themia).	Poikilocytes, Polychromato- philia. Normo- blasts. Some mi- croblasts.	Eosinophilia when due to para- sites.
PROGRESSIVE PERNIOUS ANEMIA.	Relatively in- creased. High color index.	Reduction in parallel to reds. But there may be relative lym- phocytosis.	white cells runs	Normoblasts, Megaloblasts, Poikilocytes, Polychromato- philic degener- ation. "A LARGE CELL ANE- MIA"	None.
CHLOROSIS.	Tremendously lowered. Low color index.	Unaltered.	Normal or about 4,000,000. But volume of cor- puscles reduced from normal 50 % down to 25 %.	Pessary cells, macrocytes, mi- crocytes, poly- chromatophilia, nonucleated reds, "DROPSICAL CELL ANE- MIA"	None.
SPLENO - MED- ULLARY LEUKEMIA.	Average 40 %. Average color in- dex is 0.6 %.	Tremendous leucocytosis. Polynuclear cells predominate.	Oligocythemia (Usually 10 to 40 %). Red cells approach the chlorotic type.	Normoblasts, Megaloblasts, Polychromato- philia.	Myelocytes chiefly Neuro- philic. (Normal- ly no myelocytes are found in the blood but in the bone-marrow).
LYMPHATIC LEUKEMIA.	Average 37 %.	Tremendous leucocytosis lymphocytes predominate (95 % of total white count).	Anemia of a more severe type than in the other form.	Only in severe cases do we find nucleated red cells.	None.
HODGKIN'S DISEASE.	Reduced in pro- portion to R. B. C. Very low in last stages.	Normal or else 10,000 with re- lative lympho- cytosis.	Average 3 to 4 million and in direct proportion to cachexia.	No change in red cells until late in the disease.	None.

7. SCURVY.

DEFINITION.

An acquired nutritional disease characterized by debility, anemia, spongy gums and a tendency to hemorrhage, probably due to a lack of vegetables or vegetable acids in the foods.

CLASSIFICATION.

- (A) Scorbutus or scurvy.
- (B) Infantile scurvy or Barlow's disease.

DIAGNOSIS OF SCORBUTUS.

1. **ONSET.** Very insidious. Early symptoms are:
Progressive loss in weight.
Weakness and pallor.
2. **CHANGES IN THE MOUTH.**
 - (a) Gums swollen, bleed easily, tend to ulcerate, very painful. In severe cases the gums present a fungous appearance.
 - (b) Teeth loosened and may fall out.
 - (c) Fetor oris, salivation and stomatitis.
3. **HEMORRHAGES.**
 - (a) **Mucous membranes.** Especially in mouth but not as frequent as from other places. Epistaxis is very frequent.
 - (b) **Subcutaneous.** Usually petechial in form.
Most commonly on lower extremities.
After the lower extremities are involved then the arms and trunk become involved.
The hemorrhages take place more frequently in and about the hair follicles.
Deeply situated hematoma may occur and then may ulcerate through the skin.
 - (c) **Subperiosteal.** Irregular nodes are formed.
These may also ulcerate and break through the skin.
 - (d) **Arthritic.** Hemorrhage into the joints.
4. **CACHEXIA AND ASTHENIA.**
Palpitation, feeble and irregular pulse.
Skin also becomes dry.
Severe secondary anemia. No abnormal cells.

5. **Rheumatoid arthritic pains.**

Knees and ankles most often affected.

Edema around ankles very common.

6. Advanced cases may show:

Bone necrosis and in young persons separation of the epiphysis.

Necrosis of the jaw is not common.

7. **SCURVY SCLEROSIS** oftenest seen in the legs.

It is an infiltration of the subcutaneous tissues and muscles forming a brawny induration. The overlying skin may be blood stained.

DIAGNOSIS OF INFANTILE SCURVY (BARLOW'S DISEASE).

1. **Subperiosteal hemorrhages** in the child's lower extremities occur first. The child lies motionless and its feet are kept drawn up in flexion.

These subperiosteal hemorrhages appear as ill-defined swellings.

They are not necessarily symmetrical.

Usually located around the shafts of long bones beginning above the epiphyseal junctions.

The bulk of the limb increases gradually and visibly.

2. **Pseudo-paralysis.** As the swelling progresses the lower limbs change from the original position of flexion to one of extension and eversion and the limb lies motionless and flaccid. Weakness of the back follows shortly after.

3. Swelling of one or both scapulæ may then appear.

4. Swellings in **upper extremities** are next to appear.

They are not as extensive as in the lower.

Usually seen about the wrists and in the neighborhood of the epiphysis of the humerus.

Usually symmetrical.

5. **Crepitus.** May be elicited in several cases at the junction of the epiphysis with the diaphysis.

Usual places are: upper and lower ends of femur; upper end of tibia.

6. Chest now begins to sink "en bloc."

7. Periosteal thickenings may now appear on the skull and bones of the face.
 8. **Eye symptoms.**
Proptosis of one eyeball with puffiness and staining of upper lid.
Within a few days the other eye may show the same.
 9. **Profound anemia** in proportion to the intensity of the involvement of the limbs.
 10. Emaciation is not marked but **asthenia** is pronounced.
 11. Fever. Usually 101° to 102° but very erratic.
 12. Teeth. If the teeth have appeared, the gums may be spongy.
(The essential lesion is subperiosteal blood extravasation which causes thickening and tenderness in the shafts of the long bones.)
 13. The disease usually follows the prolonged use of proprietary foods especially malted and condensed milk but may also develop in the breast-fed.
-

8. HEMOPHILIA.

DEFINITION.

A hereditary and constitutional disease characterized by a marked tendency to uncontrollable hemorrhage occurring spontaneously.

A very insignificant injury may cause a severe hemorrhage.

DIAGNOSIS.

1. By the history of "bleeders" in the family. The unaffected female is the conductor of the disease. Inherited tendency of the male to bleed.
2. **EPISTAXIS** is the usual form of bleeding in 50%.

Next in frequency is hemorrhage from the mouth and bowels.

Hematoma may form under the skin.

Hemorrhages into the joints, especially the knee cause painful anemic swellings which are liable to result in deformities and ankylosis. They are very apt to be mistaken for tubercular arthritis. These bloody effusions develop with remarkable rapidity.

3. The first hemorrhage occurs before the second year.

The early signs in children may be: umbilical hemorrhage; marked bleeding during ritual circumcision; bleeding during teething; menorrhagia in older children.

4. Coagulation of blood delayed.
5. The blood shows no typical changes other than that seen in secondary anemia due to hemorrhage).
6. "No solitary hemorrhage, however inexplicable, should be regarded as hemophilia; it is necessary to show that the individual has been repeatedly attacked, if not from birth, from infancy." (Bulloch & Fildes.)

9. PURPURA.

DEFINITION.

A symptom denoting hemorrhagic extravasation into the skin and not caused by traumatism.

CLASSIFICATION.

Petechia. Are pin-point hemorrhagic spots.

Ecchymoses. Are large spots resembling bruises.

COLOR.

All eruptions vary in color according to age of the purpuric eruption.

In the beginning they are bright red or scarlet.

Before disappearing, they pass through the various colors as seen after ordinary bruises, becoming blue-black, greenish-black or brownish.

Purpuric eruptions cannot be made to disappear on pressure.

With the absorption of the effused blood and the hematin, no trace remains to mark the site of the extravasation.

In some forms of purpura the coagulation time is retarded.

CLINICAL CLASSIFICATION (Osler).

1. SYMPTOMATIC PURPURA.

- (a) Infectious.
- (b) Toxic.
- (c) Cachectic.
- (d) Neurotic.
- (e) Mechanical.

2. ARTHRITIC PURPURA.

(a) Purpura simplex.

(e) Schönlein's disease (peliosis rheumatica).

3. PURPURA HEMORRHAGICA (Morbus maculosis Werlhof).

1. SYMPTOMATIC PURPURA.

Typhus and cerebro-spinal fevers are commonly known as "spotted fever" by virtue of the petechial rashes so commonly found in these affections. Those cases heretofore called Brill's disease are now recognized as being only typhus in a mild form. Plots has succeeded in isolating an organism (typhi-exanthematici) in typhus fever.

Embolic processes into the skin from pyemia, septicemia or ulcerative endocarditis also give rise to petechia. In the last named condition, ecchymoses may also be very marked.

Less commonly, these rashes occur in small-pox, measles and scarlet fever—the so-called hemorrhagic or "black" forms of contagious diseases which are very dangerous. These petechial eruptions and ecchymoses occur in addition to the characteristic rashes and are associated with bleeding elsewhere.

Under the toxic variety, we include snake venom, copaiba, quinine, belladonna, mercury, ergot, iodides, benzol poisoning in workers on rubber tires, etc.

The **cachectic** variety is the most common variety and is found in the cachectic states of cancer, tuberculosis, Bright's disease and in old age. The spots are in these cases usually confined to the extremities.

It may also occur in connection with organic diseases of the nervous system: tabes, myelitis and also in hysteria.

As a mechanical symptom it may be present in whooping cough, epilepsy and in venous stasis.

2. ARTHRITIC PURPURA.

(a) PURPURA SIMPLEX.

It is the mildest form and occurs most commonly in children.

Crops of petechial spots appear on the legs, especially on the flexor aspect and less commonly on the trunk and arms.

Joint symptoms are not severe.

Diarrhea usually present but no fever.

Recovery in from 7 to 10 days.

(b) **PURPURA (PELIOSIS) RHEUMATICA
(SCHÖNLEIN'S DISEASE).**

Multiple arthritis.

Many kinds of eruptions:

Usually urticaria and erythema exudativum.

Sometimes purpuric.

Often purpura and urticaria.

Rashes first appear on affected joints or on legs.

Males usually affected (20 to 30 years of age).

Articular pains are severe, especially when the rashes come out.

Fever: 101° to 103°.

Sore throat very common.

Recovery is the rule but the sore throat may persist.

VISCERAL LESIONS IN PURPURA.

May occur in any form of purpura.

(a) Gastro-intestinal crises of pain, vomiting, melæna and diarrhea so that an attack may be mistaken for appendicitis or intussusception. Purpura associated with colic is called **Henoch's purpura**.

(b) **Splenomegaly** usually present in these cases.

(c) Albuminuria and acute nephritis may occur and be the most serious symptoms.

3. **PURPURA HEMORRHAGICA. (MORBUS MACULOSIS OF WERLHOF).**

1. Includes all cases of purpura associated with hemorrhages from the mucous membranes.

2. Usually occurs in young and delicate girls but adults may also be attacked.

3. Prodromes. For a few days there may be weakness.

4. Onset. Purpuric spots on the skin which rapidly increase in size and in number.

5. Hemorrhages from any mucous membrane in the body.

Usual forms are epistaxis, hematuria and hemoptysis. Hemorrhages cause a severe anemia and may prove fatal.

6. Fever. Usually present but slight.
7. Favorable cases recover after 10 to 14 days.
8. Purpura fulminans. Death may occur within 24 hours.

This usually occurs in children.

Hemorrhages are usually cutaneous.

Death occurs even before hemorrhages occur from the mucous membranes.

10. BLOOD POISONING.

Sapremia and Septicemia.

DEFINITION.

Blood poisoning is an indefinite term and is not accepted as a cause of death. It is best described under the headings of sapremia and septicemia.

1. **SAPREMIA.** Such an infection as occurs after the retention of blood clots or fragments of membranes in the uterus after labor or abortion. The bacteria thrive on this decomposed material in the womb.
2. **SEPTICEMIA.** This is further subdivided into:
 - (A) **Toxemia or septic intoxication.** In which toxins alone are absorbed from the focus of growing pathogenic or pyogenic bacteria in the living tissues.
 - (B) **Progressive septicemia or bacteremia.** This occurs when bacteria enter the circulation.

PYEMIA. Signifies secondary multiple metastatic abscesses in the tissues during the course of septicemia.

DIAGNOSIS OF SAPREMIA.

The saphrophytic bacteria acting upon the dead material in the womb, produces toxins which are discharged into the circulation with the following results:

1. Intense chills, high fever and rapid pulse.

2. Flushed skin and dry coated tongue.
3. Change in lochia and tenderness over uterus.
4. By proper cleansing of the womb of the decomposed material all symptoms abate.
5. Usually occurs 2 to 3 days post-partum.

DIAGNOSIS OF SEPTICEMIA AND PYEMIA.

1. **Fever, chills and sweats.**

Fever is remittent in character. Highest in pyemia and in this form distinctly "septic" in character.

Chills that precede or accompany the elevation of temperature are quite severe.

The fever occurs in paroxysms but not with the same regularity as in malarial fevers.

The fever in septicemia is much lower than in sapremia and yet the patient feels worse.

The orderly sequence of chill, fever and sweat is not as characteristic as in malaria.

Diaphoresis is most marked in pyemia.

2. **Enlarged and painful spleen.**
3. **Septic diarrhea and vomiting.**
4. **Septic arthritis** is pathognomonic of pyemia. It is usually associated with skin eruptions; the most frequent being **petechia**.
5. **Septic endocarditis** is a very common complication.
6. **Septic nephritis** may occur in pyemia.

Even when nephritis does not occur the urine always contains **albumin**.

7. **Intense nervous manifestations.** There may be delirium, prostration and coma. Many pass into the so-called "typhoid state."
8. **Metastatic abscesses** as above described (in the skin, kidney, joints, endocardium) are diagnosed by an increase in the severity of the symptoms and signify pyemia.
9. **Blood.** Marked leucocytosis with an increase in percentage of polynuclear cells.

Blood cultures taken directly from a vein may show staphylococci, streptococci, colon, gonococci or pneumococci. Repeated cultures should be made if the first be negative.

11. ERYTHREMIA.

Vaquez' Disease—Polycythemia Vera.

DEFINITION.

A persistent increase in the R. B. C. associated with plethora, splenomegaly and at times cyanosis. It is a disease of the bone marrow (of the erythroblastic tissues as compared to the leucoblastic tissues in leukemia.

Hyperglobulism in consequence to high altitudes is not included under this head.

DIAGNOSIS.

1. FACIAL APPEARANCE.

Superficial blood vessels, capillaries and veins look full. Skin is therefore congested. In warm weather the face is brick-red in color. In cold, it is cyanosed.

2. SPLENOMEGALY not as great as in leukemia.

The enlargement is hard, firm and painless and may vary in size from time to time. It may cause ascites.

3. HYPERGLOBULISM.

The corpuscular volume greatly exceeds that of the plasma.

The polycythemia ranges from 7 to 12 million R. B. C. per c.mm.

Red cells are usually normal in size and shape. A few nucleated reds may be present.

Hemoglobin ranges from 130 to 160%.

Color index relatively low.

Specific gravity is high.

Moderate leucocytosis without any change in the differential count.

4. Headache, flushing, giddiness.

Constipation.

Albuminuria.

High blood pressure.

CHAPTER II.

THE BLOOD.

DEFINITION.

A fluid tissue circulating in closed vascular channels regulated by the activity of the heart and having certain well defined functions:

- (a) Nutrition. (Maintaining life).
- (b) Excretion of waste matter *via* skin and kidneys.
- (c) Regulation of body temperature.
- (d) Respiration. Its hemoglobin content forming loose combinations with oxygen and carbon dioxide.
- (e) Distribution of internal secretions.

COLOR. Due to a ferruginous substance: hemoglobin (Hb.):

Arterial blood is a bright scarlet color.

Venous blood is a purplish blue.

Bright cherry-red color occurs in certain forms of poisoning especially carbolic acid.

Brownish-red or chocolate color occurs in poisoning with chlorate of potash and aniline.

Whitish-red or milky colored blood occurs in leukemia.

Pale and watery blood is seen in hydremia and in chlorosis.

REACTION. Alkaline to special indicators.

A lowered alkalinity occurs in diabetes and is a very bad prognostic sign. During diabetic coma, the reaction may even be acid.

COMPOSITION.

Plasma—50% of the volume of the blood.

Formed elements floating in the plasma—50%.

Relation of Volume of Cells to Plasma:

By means of Daland's hematocrit which consists of 2 calibrated tubes, the divisions of which are 100 equal portions, each division approximating 100,000 cells, the blood is centrifuged and the plasma becomes separated

from the morphological elements. It gives us, therefore, a rough blood count. If the cellular portion stops at point 50 on the tube it means a red count of 5 million. ($50 \times 100,000$.)

VOLUME INDEX.

With Daland's hematocrit point 50 represents the normal, because the volume of the plasma equals the volume of corpuscles.

Supposing the cellular portion stopped at point 40. The volume per cent. would be $\frac{40}{50} = 80\%$.

Label this volume percentage "A." It is to be the numerator in the determination of volume index.

Now count the number of R. B. C. (see page 37). Suppose we counted 4,500,000. Since the normal red count is taken at 5,000,000, we must, in order to get the percentage proceed as follows:

$$\frac{4,500,000}{5,000,000} = \frac{45}{50} = \frac{9}{10} = 90\%.$$

Label this percentage "B." It is to be the denominator.

The volume index is therefore the quotient of the volume per cent. (A) as obtained by the hematocrit and the actual blood count per cent. (B). Thus, in the above instance:

$$\frac{A}{B} = \frac{\text{Hematocrit volume of red cells in } \%}{\text{Percentage counted red blood cells}} = \left\{ \begin{array}{l} \text{Volume index of red} \\ \text{cells.} \end{array} \right.$$

Then inserting figures: $\frac{80\%}{90\%} = \frac{8}{9}$. Normally it is 1.

According to Capps, this volume index is constantly increased in pernicious anemia. The color index never exceeds the volume index. In primary and secondary anemias this factor is decreased and oftentimes the color index falls below the volume index. Color index is described on page 38.

COMPOSITION OF BLOOD PLASMA.

Plasma is the liquid portion of the circulating blood. When blood clots (see page 52) the liquid which exudes from the clot is called serum.

Serum consists of:

- { Proteids: serum albumin and serum globulin.
- { Glucose, extractives, calcium salts, sodium and potassium chlorides, carbonates, phosphates, etc.

The chief **extractives** are:

Fat, sugar, urea, uric acid, sarco-lactic acid, lecithin, cholesterin, glycuronic acid, creatin, carbamic acid, glycogen, hippuric acid.

THE MORPHOLOGICAL OR FORMED ELEMENTS OF THE BLOOD.

- { Red cells (R. B. C.).
- { White cells (W. B. C.).
- { Blood plates.

ENZYMES in the blood.

- { Glycolytic ferment.
- { Lipolytic ferment. (Fat synthetizing.)
- { Oxidases.
- { Proteolytic properties of leucocytes.
- { Internal secretions as adrenalin, etc.
- { Amboceptors.
- { Complements.

GASES of the blood.

- { Oxygen.
- { Carbon dioxide.
- { Nitrogen.

Arterial blood.	Venous blood.
Oxygen. 21.6%	6.8%
Carbon dioxide. 40.3%	48.0%

BLOOD PRESSURE.

NORMAL FIGURES. (Janeway's).

Infants. 75 to 90 mm. Hg.	} Maximum systolic
Children over 2 years. . . . 90 to 110 mm. Hg.	
Young adults. 110 to 130 mm. Hg.	
Older adults 110 to 145 mm. Hg.	

HOW TO OBTAIN NORMAL B. P.

Consider a person aged 20 as having a B. P. of 120.
for every 2 years above this age add 1 mm. Hg.

Hence:—

At 40, the B. P. would be 130 mm. Hg.

At 50, the B. P. would be 135 mm. Hg.

Permissible variations which occur normally.

Seventeen mm. Hg. above or below would be the normal figure for any given age.

THE SPHYGMOMANOMETER IN LIFE INSURANCE.

1. In those applicants who are overweight the blood pressure tests determine whether the company should take the risk.
2. It is a recognized fact that **permanent** changes in the kidney cannot exist without causing an increase in the B. P. So that, if an applicant does show a faint trace of albumin and casts are present in scanty numbers, this evidence alone will not cause an absolute rejection unless his B. P. is decidedly increased.
3. Signs of beginning pathological change in the cardiovascular-renal system can be recognized by this instrument long before we can demonstrate any abnormal findings in the heart, pulse or urine.
4. A blood pressure exceeding 145 in a person before middle life, or a reading of 160 after middle life has passed must be considered as abnormal. (Janeway).

TO OBTAIN THE MAXIMUM SYSTOLIC B. P.

To obtain the **maximum systolic** blood-pressure a broad arm piece should be used. When the pulse at the wrist is obliterated the height of the mercury column is equivalent to the maximum systolic pressure. Many observers claim that it is better to accept the reappearance of the radial pulse after obliteration than the initial disappearance of the radial pulse. The Janeway apparatus and the Tycos' sphygmomanometer are best recommended. The **minimum diastolic** blood-pressure is obtained by letting the pressure fall 5 mm. Hg. at a time and at the same time watching the amplitude of the pulsations of the mercury column or oscillations of the needle—and at that point where the greatest amplitude occurs, that point registers the diastolic blood-pressure.

The auscultatory method may also be employed.

HYPOTENSION.

Definition: A blood pressure reading that is lower than what it should be at any given age and under ordinary conditions.

In recent years hypotension has come to be looked upon as both a diagnostic and a prognostic factor. If one will only

HYPERTENSION.

Definition: A very noticeable increase in blood pressure above the average for any given age. It may reach the 300 mark and it may be temporary or permanent. It is only a symptom and it is our duty to investigate the cause. It is also well to re-

HYPOTENSION.

bear in mind that whenever vaso-dilatation occurs in consequence to a vaso-motor paresis, the blood vessels become excessively dilated and consequently the blood pressure falls, it will be very easy to interpret the meaning. Such a vaso-motor paresis is the cardinal factor in **shock** and **collapse**. In these conditions the greater the fall in blood pressure the more dangerous does the patient's condition become.

Hypotension is a recent additional diagnostic point in **typhoid fever**. In fact, of all the acute infections which may be accompanied by a low pressure, typhoid ranks first and pneumonia second. It has also been noticed here that the hypotension bears a relation to the toxic symptoms. As the intoxication increases (provided certain complications are absent) the blood pressure falls (vaso-motor paresis). On the other hand with the advent of a complication like a perforative peritonitis the blood pressure will rise. Then, again, the blood pressure reading will easily differentiate between a hemorrhage of the bowel and a perforation followed by peritonitis. Intestinal hemorrhage is always accompanied by a low blood pressure, whereas perforative peritonitis causes an elevation of blood pressure.

HYPERTENSION.

member that it is often a salutary and beneficent condition not to be interfered with.

A patient whose arterial tension exceeds 260 mm. Hg. is liable to die suddenly.

The usual causes of hypertension are found resident either in the cardio-vascular system or in the kidneys. A good working rule is as follows: A **permanent** increase in blood pressure in a young adult or in one in early middle life, in the absence of organic changes in the heart, blood vessels or kidneys, must be explained by the presence of a **chronic toxemia**, or a poisoning arising from some error in metabolism, either intestinal, urinary or both. With the advancement in years the blood pressure naturally increases progressively.

The Sphygmomanometer also has its uses in **obstetrics**. It has been employed to detect the development of the toxemias of pregnancy and nephritis occurring in those conditions. After exhaustive clinical study, we must conclude that the taking of blood pressure readings is just as important as the repeated urinary examinations and pelvimetry in pregnancy. In these cases, where hypertension is found, we can explain its presence by a toxemia by virtue of the metabolic waste products being absorbed in the system. As far as it is

HYPOTENSION.

In passing it may be stated that Barach has found the blood pressure in enteric fever usually below the century mark, and it does not bear any relation to the pulse rate nor the temperature.

Before dismissing the subject of hemorrhage, it is well to remember that with the exception of cerebral hemorrhage, all other hemorrhages (either visible or concealed) must be accompanied by a lowering in pressure. The lowering is in direct proportion to the quantity of blood lost. However, in favorable cases where regeneration of the blood takes place, the volume of the blood (its watery constituent) is soon restored almost to normal, the hypotension is only short lived. It is, therefore, a valuable prognostic as well as diagnostic feature.

Returning to pneumonia, we may state that we are also dealing with an intoxication which may cause vascular paresis. The best way to detect such a failure in the circulation is by daily and frequent blood pressure readings. Circulatory depression in consequence of such a toxemia is always accompanied by a fall in blood pressure, whereas it has been noted that typhoid bears no relation between the pulse rate and the blood pressure, we do find in pneumonia such a correlation. According to Gibson, the situa-

HYPERTENSION.

possible to lay down rules in these cases, we may say that a blood pressure below 125 could be disregarded; a pressure from 125 to 150 needs careful watching and moderate eliminative treatment; and that a pressure over 150 needs very active eliminative treatment and will, in all probability, especially if it shows a tendency to climb higher, require the induction of premature labor.

In concluding the subject of hypertension, the diagnostic value of this phenomenon can readily be seen in cases of cerebral hemorrhage. This increased blood pressure is the most reliable and diagnostic sign. It is readily differentiated from cerebral embolism by the fact that this latter condition is accompanied by a low pressure. The elevation of the blood pressure in cerebral hemorrhage bears a direct relation to the increase in intracranial tension so that in cases where the hemorrhage increases in size the pressure increases in proportion. On the other hand, if the cranial encroachment is a slow and chronic process like a tumor there is no effect upon the blood pressure. Finally, as before stated, cerebral hemorrhage is the only hemorrhage which is accompanied by hypertension; all other forms of hemorrhage are accompanied by a diminution in blood pressure.

HYPOTENSION.

tion in pneumonia may be summed up as follows: "When arterial pressure expressed in millimeters of mercury does not fall below the pulse rate expressed in beats per minute, this fact may be taken as excellent augury, while the converse is equally true."

Although a high blood pressure is invariably associated with aortic regurgitation, it is only valvular disease which has hypertension as a diagnostic feature. In all the other valvular lesions, as well as all organic lesions of the heart, we find hypotension.

Emerson's findings in tuberculosis of the lungs is as follows: Hypotension in pulmonary tuberculosis is (1) a very marked and constant factor in advanced cases; (2) present but not so very marked in moderately advanced cases; (3) and it can oftentimes be demonstrated in the incipient stage, and even before the development of physical signs. Therefore, it may be inferred that the longer the disease has existed the more marked will the lowering in blood pressure be. He also claims that in those cases where the trend is towards recovery we will note a progressive return to a normal pressure.

We are very frequently called upon to differentiate the various forms of coma and the

HYPOTENSION.

task is not always very easy. Edgecombe has remarked the noticeable frequency of hypotension in epileptic coma in contrast to hypertension which accompanies uremia.

In conclusion, it is well to add that wherever life is low as in cachectic states, the blood pressure tends to fall progressively.

SPECIFIC GRAVITY. Varies from 1.050 to 1.062.

In children it is nearer to 1.050.

The average is 1.055.

According to Schmaltz, the sp. gr. is in direct relation to the amount of hemoglobin and the volume of the red cells (excepting in nephritis, circulatory disturbances, leukemia, post-hemorrhagic anemia and inanition. His figures are:

With a sp. gr. of 1.059	Hb. is 100%
With a sp. gr. of 1.0575	Hb. is 90%
With a sp. gr. of 1.056	Hb. is 80%
With a sp. gr. of 1.0535	Hb. is 75%
With a sp. gr. of 1.052	Hb. is 70%
With a sp. gr. of 1.051	Hb. is 65%
With a sp. gr. of 1.049	Hb. is 60%
With a sp. gr. of 1.048	Hb. is 55%
With a sp. gr. of 1.0455	Hb. is 50%
With a sp. gr. of 1.0425	Hb. is 45%
With a sp. gr. of 1.041	Hb. is 40%
With a sp. gr. of 1.038	Hb. is 35%
With a sp. gr. of 1.035	Hb. is 30%
With a sp. gr. of 1.030	Hb. is 20%

Hammerschlag's Method of Determination of Sp. Gr.

Make a mixture of chloroform (sp. gr. 1.526) and benzol (sp. gr. 0.889) so that it is almost like that of normal blood (1.050 to 1.062).

A drop of fresh blood from a capillary blood pipette is allowed to fall into this mixture. It will either sink or rise. If it sinks to the bottom, add chloroform drop by drop; and if it rises or floats add benzol drop by drop; until the drop of blood remains stationary in the mixture. Filter very quickly because evaporation will occur, and read the sp. gr. by means of a hydrometer inserted into the mixture.

RED BLOOD CORPUSCLES. (ERYTHROCYTES.)

MORPHOLOGY.

1. In mammals, they are flat, circular, non-nucleated discs, $7\frac{1}{2}$ microns or $1/3200$ of an inch in diameter, having a pale central area.

In fresh blood, the red cells show a tendency to "coin-roll" formation.

As fresh blood dries upon the slide, the red cells become crenated; that is to say, spinous projections from the cell appear like a cogged rim.

2. In birds, reptiles, amphibians, camels, they are bi-convex, oval and nucleated. The largest cells are found in the amphibia.

PATHOLOGICAL RED CELLS.

1. Pessary or ring cell.

Large pale central area with a small rim of protoplasm. They are called "dropsical cells" and are very diagnostic of chlorosis.

2. Nucleated red cells.

- (A) **Normoblasts.** (Trachyochromatic erythroblasts).

A matured normoblast can thus be recognized:

Size and shape about that of a normal R. B. C., but it has a nucleus. If a trifle smaller in size it is called a microblast.

Both together signify REGENERATION of the blood and are especially found after hemorrhage.

Normoblasts stain more intensely.

Its nucleus is about one-third of its diameter. It is densely stained, more homogenous, sharply defined, spheroid and devoid of chromatin network. It is usually situated towards the periphery.

An immature normoblast shows a very distinct network, is larger and lighter in color and the chromatin fibers are radially arranged and frequently shows mitotic figures. (Howell.)

- (B) **Megaloblasts.** (Amblyochromatic erythroblasts).

Size: larger than normoblasts.

Protoplasm: usually swollen and enlarged.

Hemoglobin: as a rule in excess.

(For Drawings)

Usually psychromatic, the shade of the stain varying from yellow to purple.

Nucleus: very large, varying from 6 to 10 microns and may assume many forms. As a rule it is ill-defined and shows feeble basic staining properties.

Megaloblasts signify abnormal DEGENERATION.

They appear in leukemia, pernicious anemia, infection with the *Bothriocephalus Latus*, nitrobenzol poisoning, severe anemia, etc.

When the nucleus of a nucleated R. B. C. exceeds 20 microns it is termed **gigantoblast of Ehrlich**.

3. **Poikilocytosis.** The simultaneous variation in both size and shape of the red cells. It is very characteristic of pernicious anemia.
4. **Microcytes and macrocytes.** The normal sized R. B. C. is also called a normocyte. If a cell is a little smaller it is a microcyte. If a little larger than a normocyte, it is a macrocyte. These cells occur in grave and in pernicious anemia.
5. **Polychromatophilia or polychromasia.**

The normal red cells, when a smear is **fixed** and stained, stains only with acid dyes. Hemoglobin is therefore said to be acidophilic.

Abnormal red cells not only show affinity for acid dyes but basic dyes. These red cells instead of appearing monochromatic (one color) will appear with several colors: gray, slaty, purple, violet, etc.

There are two distinct forms:

Polychromatophilic degeneration of Gabritschewsky. In which there is a diffuse basophilic staining of the cells.

Polychromasia of Maragliano in which the basophilia is **punctate**. It is very closely related to the basophilic degeneration of Grawitz.

6. **Basophilic degeneration.** (Grawitz.) Granules of varying size appear in the body of the R. B. C. and stain with basic dyes. Very diagnostic of lead poisoning. It is also common in diabetes, myelogenous leukemia, pernicious anemia, severe secondary anemias especially those following malignant disease, eruptive fevers and malaria.

7. **Microcyte** is a red cell smaller than a normal cell. Diameter varies from $3\frac{1}{2}$ to 6μ .
8. **Macrocyte** is a cell larger than a red cell. Size varies from $9\frac{1}{2}$ to 12μ .

NUMBER OF RED BLOOD CELLS.

Males: 5,000,000 per c.mm.

Females: 4,500,000 per c.mm.

Oligocythemia: Pathological reduction in number. As a rule there is a corresponding decrease in Hb.

It occurs in nearly all forms of anemia and as a result of the toxins of specific fevers.

Polycythemia (Polyglobulia): increase in number of R. B. C.

1. High altitudes. 50,000 cells for every 1000 feet ascension.
2. Watery diarrheas.
3. Severe diuresis and ascites. Numbers 2 and 3 cause increased concentration of the blood.
4. Cardiac diseases. All forms of cyanosis.
5. Drugs causing vaso-constriction.
6. Diseases of the adrenal glands.
7. Phosphorus poisoning and acute yellow atrophy of the liver.
8. Hepatic insufficiency.

COUNTING THE NUMBER OF R. B. C.

Prick the tip of finger or ear, and with blood pipette No. 101, draw blood up to the 0.5 mark.

Now draw enough Hayem's solution up to 101 mark and shake vigorously for at least one minute. This gives a 200 dilution.

Discard the first few drops and then **blow** one drop on to the center piece of the Thoma-Zeiss hemocytometer and adjust the special cover-slip carefully in place until Newton's rings are visible.

Examine first with low power lens to see if the red cells are evenly distributed. If not make a new specimen.

With high power lens, begin at upper left-hand corner and proceed downward, being guided by the ruled lines, then upward, then down again and count the number of R. B. C. in 80 squares. To this factor add 4

ciphers. Providing the dilution is 200, this number represents the number of red cells per c.mm. If we counted 325 cells, the count would be 3,250,000.

If blood has been drawn past the 0.5 mark, for example 0.6, proceed as follows: Divide the number of red cells counted in the 80 squares by the division stopped at and multiply by 5000. Suppose we counted 390 cells. Dividing this by 0.6 we get 650. Then 650x5000 equals 3,250,000.

Hayem's Solution consists of:

Bichloride of mercury.	0.5
Sodium sulphate.....	5.0
Sodium chloride.....	1.0
Distilled water.....	200.0

Owing to the presence of bichloride, the fluid cannot be mixed with an aniline coloring substance to stain the leucocytes, and it is therefore not applicable to the combined counting of red and white cells.

Toisson's Fluid consists of:

Sodium chloride..	1.0 G.
Sodium sulphate..	8.0 G.
Neutral glycerine.	30.0 c.c.
Distilled water...	160.00 c.c.
Methyl violet 5 B.	.025 G.

This colors the white cells and with it both red and white cells can be counted. Objections to this fluid are (1) it may cause hemolysis at times; hence the red count is worthless; (2) spores develop readily in it and in order to use it must first be filtered. Each filtration further weakens the solution.

COLOR INDEX. (Value of corpuscles.)

Represents the relative amount of hemoglobin contained in each red cell as compared when a normal number of erythrocytes obtains. In other words, it is the quotient of the percentage of Hb. divided by the percentage red cells. The latter factor is obtained by dividing the number of red cells counted by 5 million.

Examples:

What is the color index when one counts 2,500,000 red cells and the Hb. is 50%?

$$\frac{2,500,000}{5,000,000} = \frac{1}{2} = 50\%; \text{ and } \frac{50}{50} = 1 = \text{Color Index.}$$

What is the color index when one counts 3,000,000 red cells and the Hb. is 40%?

$$\frac{3,000,000}{5,000,000} = \frac{3}{5} = 60\%; \text{ and } \frac{40}{60} = \frac{2}{3} = \text{Color Index.}$$

What is the color index when one counts 1,500,000 red cells and the Hb. is 45%?

$$\frac{1,500,000}{5,000,000} = \frac{3}{10} = 30\%; \text{ and } \frac{45}{30} = 1\frac{1}{2} = \text{Color Index.}$$

A very simple method of obtaining the percentage of red cells of the normal 5,000,000 is to multiply the number of hundreds of thousands of the red cells counted by two. Thus if 2,650,000 cells were counted, we multiply 265 by 2. This equals 53%.

WHITE BLOOD CORPUSCLES. (LEUCOCYTES.)

MORPHOLOGY. In the fresh specimen, they appear as highly refractive, nucleated cells, having a variable amount of clear or granular cytoplasm, possessed of ameboid movement with a phagocytic property. They are larger than the R. B. C.

CLASSIFICATIONS.

1. Mixed or present classification of today:

- (a) Polymorphonuclear neutrophile.
- (b) Lymphocytes: large and small.
- (c) Mononuclear.
- (d) Transitional.
- (e) Polynuclear eosinophile.
- (f) Polynuclear basophile (mast cell).

2. According to granules:

- (a) Granular.....
 - { Polymorphonuclear neutrophile.
 - { Eosinophile.
 - { Basophile.
 - { Myelocyte.
- (b) Non-granular..
 - { Lymphocytes.
 - { Mononuclear.
 - { Transitional.

3. According to nuclei:

- (a) Polynuclear...
 - { Neutrophile.
 - { Eosinophile.
 - { Basophile.
- (b) Mononuclear....All the rest.

4. According to staining of protoplasm:

- (a) Neutrophile.
- (b) Eosinophile.
- (c) Basophile.

LEUCOCYTES DESCRIBED.

- (a) **POLYMORPHONUCLEAR NEUTROPHILE.** (Finely granular cells of Schultze.)

Constitute 65 to 75% of the total white cells.
Twice as large as a red cell.

Nucleus or rather nuclei vary greatly in shape and are stained blue (basophilic).

Protoplasm contains numerous irregularly placed and irregular sized granules stained pink (acidophilic).

When outside the blood vessels they form pus.

- (b) **LYMPHOCYTES.**

Constitute 20 to 30% of the total W. B. C.

Large lymphocyte.

One and one-half times the size of R. B. C.

Nucleus deeply stained.

Has more cytoplasm than a small lymphocyte.

Small lymphocyte.

Is about the size of a red cell.

Its nucleus also deeply stained.

Has a small rim of cytoplasm.

- (c) **LARGE MONONUCLEAR.**

About 3 times as large as a red cell.

Has a round or oval faintly stained nucleus, which is basophilic.

Considerable reticulated cytoplasm, few meta-chromatic granules.

- (d) **TRANSITIONAL.**

(c) plus (d) equal 6% of the total W. B. C.

These cells resemble the former excepting that the nuclei are kidney shaped (notched) and pale.

- (e) **POLYMORPHONUCLEAR EOSINOPHILE.** (Coarsely granular cells of Schultze.)

Constitute about one-half to 3% of total W. B. C.

Is as large as a polymorphonuclear cell.

Has large, coarse, red granules arranged in mosaic form in its protoplasm. It stains with acid dyes. The nuclei are coarsely reticulated, usually bilobed, and rather indistinct.

(For Drawings)

(f) **POLYMPHONUCLEAR BASOPHILE OR MAST CELL.**

Constitutes one-half per cent. of total W. B. C.
Is as large as a polymorphonuclear cell.

Nucleus is indistinct.

Cell appears as if it were bespattered with ink.

It also has metachromatic granules.

The mast cells are best stained by Ehrlich's dahlia stain or by Turk's iodine method.

NUMBER OF LEUCOCYTES.

Normally: 5,000 to 10,000 per c.mm. Average 7,500.

Leucopenia: Reduction in total white count.

Leucocytosis: Increase in total white count. May be

(a) **Absolute:** Increase in total number of W. B. C.

(b) **Relative:** A proportionate increase of any given variety of colorless corpuscles, the total white count remaining unaltered.

CLASSIFICATION OF LEUCOCYTOSES (Modified after Limbeck).

1. PHYSIOLOGICAL LEUCOCYTOSIS.

(a) **Digestive.** Unless cancer of the stomach exists a leucocytosis of the polynuclear type averaging 10,000 occurs after eating.

(b) **Pregnancy.** Average count is 15,000.

Occurs in more than 50% of the cases.

Especially marked in primiparæ.

All the white cells excepting eosinophiles are increased. (Mixed leucocytosis.)

Count returns to normal within 10 to 14 days after delivery providing no such complications like fever, hemorrhage, etc., arise.

(c) **New-born.** Average 15 to 20 thousand.

Disappears as child begins to gain in weight.

The small mononuclears constitute 40 to 60% of total W. B. C.

2. PATHOLOGICAL LEUCOCYTOSIS.

(a) **Inflammatory.** All forms of suppurative inflammation except when an abscess is well walled off. In septic conditions the polymorphonuclear cells predominate.

The common diseases associated with leucocytosis are: acute lobar pneumonia, acute articular rheumatism, scarlet fever, whooping cough, erysipelas, cerebro-spinal meningitis, pus infections, etc.

- (b) **Cachectic** (due to malignant tumors).

More often after cancer than sarcoma.

- (c) **Posthemorrhagic**. Polymorphonuclear cells predominate. White count may reach 20,000 within one hour after a severe hemorrhage. It is, however, transient, disappearing long before regeneration of the blood has occurred.
3. Leucocytosis from medicinal and therapeutic measures: baths, drugs, exercise.
 4. Leucocytosis from other causes: cyanosis, shock, vaccine injections, etc.

MIXED LEUCOCYTOSIS.

An increase in both granular and non-granular cells but its more common interpretation is an increase in the number of **neutrophile myelocytes**. Best seen in spleno-myelogenous leukemia. In no other conditions excepting leukemia do we ever find more than 1,000 myelocytes. In leukemia it may reach 150,000.

SIGNIFICANCE OF RELATIVE LEUCOCYTOSES.

EOSINOPHILIA. To be called a true eosinophilia there must be over 250 such cells per c.mm.

- (a) Parasitic infections: as trichinosis, intestinal worms, hydatids, chronic malaria.
- (b) Bronchial asthma at time of paroxysm.
- (c) Spleno-myelogenous leukemia.
- (d) Many skin diseases. Seems to depend more upon extent of lesions than upon nature. Common diseases are: pemphigus, urticaria, purpura, eczema, psoriasis.
- (e) Bone diseases: osteomyelitis, osteomalacia, sarcoma.
- (f) Malignant disease.
- (g) Gonorrhea: both in blood and discharge.

LYMPHOCYTOSIS.

- (a) Children. From birth up to puberty the lymphocytes constitute 50 to 65% of W. B. C. Gradual reduction to the normal 20 to 30% by the time puberty is reached.

(b) Lymphatic leukemia.

Acute forms: large lymphocytes predominate.

Chronic forms: small lymphocytes predominate.

(c) Typhoid. Uncomplicated cases show leucopenia with lymphocytosis.

(d) Syphilis. Also found in the spinal fluid in syphilitics.

MYELOCYTOSIS. A myelocyte is a mononuclear cell which is distinctly granular. These granules are usually **neutrophilic** or **eosinophilic**. But in myelogenous leukemia they may be basophilic. The size of myelocytes varies from that of a R. B. C. to a large mononuclear. The myelocytes are not **normally** found in the circulation but they are found in the bone-marrow.

(a) Spleno-myelogenous leukemia.

(b) Pernicious anemia.

(c) Bone disease: syphilis, tuberculosis, tumors.

(d) Malignant tumors of gastro-intestinal tract.

(e) Empyema in children.

(f) Some acute infectious diseases:

Lobar pneumonia (8 to 12%).

Diphtheria: (bad prognosis).

LEUCOPENIA. White count reduced below 5,000.

(a) Typhoid: uncomplicated cases only.

(b) Measles: after the rash.

(c) Malaria: but lymphocytes may be slightly increased.

(d) Tuberculosis.

(e) Mumps unless suppuration of the gland occurs.

(f) Starvation and malnutrition.

(g) Chronic poisoning with heavy metals, morphine, alcohol, cocaine.

(h) Grippe if uncomplicated. Thus, can be diagnosed from pneumonia in which leucocytosis occurs.

(i) Pernicious anemia and splenic anemia.

COUNTING THE WHITE CELLS.

Draw blood up to 0.5 mark in pipette No. 11.

Draw up sufficient amount of 0.5% acetic acid solution up to the 11 mark. (Acetic acid destroys R. B. C.)

Examine as described under red cells (page 37), but count the entire 400 squares and use low power lens.

The dilution as given above is 20.

To find the number of W. B. C. multiply the number of cells counted in all the squares by 20 and then by 10 (the depth of the examining chamber). In other words, multiply the number of cells counted by 200.

If blood be drawn past the 0.5 mark, divide the number of cells counted by the division at which we stopped and multiply by 100.

Suppose we counted 42 cells in 0.6 c.c. blood. Therefore $\frac{4.2}{0.6} \times 100 = 7,000$ W. B. C.

DIFFERENTIAL WHITE COUNT.

First ascertain the total white count as above.

Make a thin blood smear, fix, stain and examine with a microscope. (Wright's stain is best for differential count).

Count 200 leucocytes and as each one is seen place a mark along the side of the name of the cell in the list as arranged below:

{	Polymorphonuclear neutrophile.
	Large lymphocyte.
	Small lymphocyte.
	Mononuclear.
	Transitional.
	Polymorphonuclear eosinophile.
{	Polymorphonuclear basophile.
	Unclassified cells.
[	Pathological cells.

Now then, assuming that 150 polymorphonuclear neutrophiles were counted in the 200 squares the percentage therefore is 75. The percentages for the other cells are determined in a similar manner.

BLOOD SMEARS: Preparation and staining.

Cleanse part from which blood is to be drawn.

Puncture skin with a Hagerdorn needle and wipe off the first drop of blood which appears.

Apply a clean slide to the bleeding point and permit one drop to adhere to the slide at a point about $\frac{3}{4}$ -inch from the smaller edge of the oblong slide.

With another clean slide, held at an angle of 45° , bisect this drop and wait until the blood has spread along this angle by capillarity.

When the angle has almost completely been covered draw the second slide across the first using firm and steady pressure. The object is to get a thin smear.

Before any of the morphological elements of the blood can take up any stain the smear must first be FIXED by any process which will coagulate the proteid constituent of the blood.

The air dried film is exposed to heat or to chemicals. Fixation by methyl alcohol (C. P.) for 3 to 5 minutes is one of the best methods.

STAINS FOR ROUTINE PURPOSES.

- | | | |
|--------------------------|---|---|
| 1. Eosin-methylene blue. | { | These stains are the best because they are simple in technic and show clear-cut pictures of all the important blood elements. |
| 2. Eosin-hematoxylin. | | |
| 3. Wright's stain. | | |

1. EOSIN-METHYLENE BLUE STAIN.

1. Fix smear in pure methyl alcohol for 3 minutes (If we find later that the nuclei are indistinct fix for a longer period.)
2. Stain in $\frac{1}{2}\%$ alcoholic (70%) solution of Grübler's "French pure" eosin for 3 to 5 minutes. (This brings out the neutrophilic granules distinctly).
3. Wash in distilled water and dry between filter paper.
4. Deposit slide for $\frac{1}{2}$ to 1 minute in a small bath containing:
20 drops of a $\frac{1}{4}\%$ aqueous solution of methylene blue (B. pat), and
10 drops of the above eosin solution.
5. Quickly wash (briefly) with distilled water.
6. Dry at once between filter paper or over flame.
7. Mount if desired in Canada Balsam or examine directly with high power lens.

With this stain the morphological elements are thusly recognized:

R. B. C. and eosinophilic granules of W. B. C.: bright red.

Neutrophilic granules: pink to bright red.

(The granules being smaller than that of the eosinophiles.)

Nuclei, mast-cell granules, bodies of lymphocytes, platelets, malarial organisms, trypanosomes and filaria: varying shades of blue.

Note.—For malaria it is not a very good stain because it does not stain the chromatin very good. It is better than any of the Romanowsky's stains or its modifications.

2. EOSIN HEMATOXYLIN STAIN.

Best adapted for examination of nuclear structures.

Two solutions are required.

Stain with solution No. 1 for $\frac{1}{2}$ minute.

Wash in water but do not dry.

Deposit slide in solution No. 2 for 1 to 3 minutes.

Wash in water, dry and mount.

Solution No. 1. $\frac{1}{2}\%$ Grübler's blood eosin in 70% alcohol.

Solution No. 2. Delafield's hematoxylin solution which consists of:

Hematoxylin crystals.....	4 G.
Absolute alcohol.....	25 c.c.
Ammonium-alum crystals C. P.....	52 G.
Distilled water.....	400 c.c.
Glycerine, C. P.....	100 c.c.
Methyl alcohol, C. P.....	100 c.c.

HOW TO PREPARE DELAFIELD'S HEMATOXYLIN SOLUTION:

1. Rub up hematoxylin crystals with alcohol until dissolved.
2. Place this solution in a loosely corked bottle and permit to stand 4 days exposed to the light.
3. Dissolve the ammonium-alum crystals in 400 c.c. water and allow to stand as the above.
4. After 4 days mix both bottles and shake vigorously.
5. After 3 hours, filter.
6. Now add the glycerine and methyl alcohol to the filtrate and allow this to stand over night.
7. Filter this mixture again, catching the filtrate in a clear bottle. After standing in the light for six weeks it ripens and is ready for use.

3. WRIGHT'S STAIN.

1. Flood the smear with the stain for one minute. A definite number of drops should be dropped on the slide by means of a medicine dropper.

2. Add the same number of drops of distilled water. (See that no fluid runs off by using proper amounts.) (It stains the eosinophilic granules beautifully.)
3. Wash in water for 30 seconds, or until the thinner portion of the film becomes yellow or pink.
4. Dry between filter paper; mount if desired and examine.

Note.—for malarial parasites the decolorization should not be so long because it affects the chromatin.

The formed elements are thusly colored:

R. B. C.....	orange or pink.
Nuclei of W. B. C.....	blue or dark lilac.
Neutrophilic granules.....	lilac.
Eosinophilic granules.....	red or pink.
Fine basophilic granules.....	deep blue.
Large mast-cell granules.....	purple
Protoplasm of lymphocytes.....	robin's-egg blue.
Bacteria.....	blue.
Malarial and other parasites.....	blue.

(The chromatin elements varying from lilac to ruby-red to black.)

Polychromatophilia and granular degenerations.blue.

PREPARATION OF WRIGHT'S STAIN.

Place into a suitable flask 1 G. methylene blue (B. X. or "medicinally pure") for every 100 c.c. of 0.5% solution of sodium bicarbonate.

Heat this mixture for 60 minutes in a steam sterilizer at 100° C. After heating, permit to cool.

Filter and remove the precipitate.

To each 100 c.c. of the filtered mixture add 500 c.c. of a 0.1% aqueous solution of "yellowish, water-soluble" eosin and mix thoroughly.

Collect the abundant precipitate (which appears immediately) on a filter.

When this precipitate is dry dissolve in methyl alcohol (Merck's reagent) in the proportion of 0.1 G. to 60 c.c. of alcohol.

This is the stain and should be kept well stoppered to prevent evaporation of the alcohol.

HEMOGLOBIN. (Hb.)

A complex proteid containing iron. It is the pigment which gives color to the blood. It forms loose combinations with oxygen and plays an important part in respiration.

AMOUNT. For every 100 c.c. blood we find on an average of 13.77 G. Hemoglobin (symbol Hb.). In man it is nearer to 14 G. In women it is nearer 13 G.

Clinically 14 G. is regarded as 100%.

The estimation of the percentage hemoglobin is arrived at by comparing the color of that patient's blood to certain standard solutions of blood or standardized color charts or scales. The hemoglobinometers recommended are Fleischl-Miescher's, Sahli's, Gower's, Dare's, Oliver, Tallqvist's, etc.

(The reader is now referred to page 38 for the discussion of "color-index," and to Schmaltz's figures for percentage Hb. based upon specific gravity. P. 33.)

HEMOGLOBINEMIA AND HEMOGLOBINURIA.

Normally red cells are being constantly disintegrated but is very insignificant.

Under certain conditions the destruction is so rapid and the blood pigment accumulates so rapidly in the blood (hemoglobinemia) that the liver is unable to convert it into bilirubin. With hemoglobinemia there must be hemoglobinuria (the pigment passes out through the urine).

It may occur in the following conditions:

1. **Poisoning.** Phenol, chlorate of potash, pyrogallie acid, antimony, hydrochloric and sulphuric acids, coal-tar products, sulphonal, etc., either by hypodermic injections or large doses internally.
2. **Certain diseases.** Scarlatina, typhoid, intermittent fever, icterus gravis, syphilis.
3. After transfusions of the blood of animals into man, and after severe burns and exposure to cold.
4. **Anesthetics** are also hemolytic poisons.

Urine. The urine in hemoglobinuria is usually turbid. Varies in color from bright red to almost black. It must not be confounded with hematuria. Chemical tests cannot differentiate them. Micro-

scopically in hematuria we find the red blood cells. In hemoglobinuria the urine should be immediately centrifuged. Few or no red cells should be in the sediment.

TESTS FOR HEMOGLOBIN AND DERIVATIVES.

(A) HELLER'S TEST.

1. Add NaOH to a few c.c. of urine so as to make it strongly alkaline.
2. Heat. A brownish-red precipitate is thrown down. Color due to the presence of hematin. Precipitate consists of the phosphates and carbonates of the alkaline earths.
3. In case the urine contains a large amount of foreign pigment, the red cells may not be easily noted.

In that case, filter off the precipitate and redissolve it in acetic acid. In the presence of blood it becomes red but fades on standing in the air.

Note.—This test will indicate one part oxy-hemoglobin in 4,000 urine.

(B) DONOGANY'S TEST.

1. To 10 c.c. urine add 1 c.c. ammonium sulphide and 1 c.c. pyridin. In the presence of blood the urine becomes orange-colored.
2. Hemoglobin having thus been converted into **hemochromogen** we can recognize same by its characteristic absorption bands. (See page 94.)
3. This test shows one part blood to 8,000 of urine.
4. If the urine contains fresh blood, the spectrum will be that of oxyhemoglobin while in case of hemoglobinuria or of hematuria of renal origin, the spectrum is that of methemoglobin. (Webster.)
5. For the spectroscopic examination of urine it is necessary that the urine be acid.

PAROXYSMAL HEMOGLOBINEMIA.

1. Cause is unknown but usually follows catching cold.
2. Attack is paroxysmal and ushered in by persistent yawning, pain in limbs, headache, nausea and vomit and coolness of the periphery.

3. Temperature quickly rises to 102° and is associated with a severe chill.
4. Severe hepatic pains at times.
5. Splenomegaly very characteristic.
6. Slight jaundice towards end of the attack.
7. After 10 to 12 hours, the fever falls and is followed by sweating.
8. Urticarial eruptions frequently seen during attack.
9. **Urine very characteristic.** (During and directly after the paroxysms.)

Color: varies from brownish-red color to black.

Reaction: invariably acid.

Specific gravity: usually low: 1008-1012.

Boiling: will decompose the Hb. and a brown coagulum of albumen is formed.

Spectroscopy: fresh urine shows Hb. spectrum and sometimes that of methemoglobin.

Casts: usually present. (Hyaline and some containing hemoglobin granules.)

NO RED BLOOD CELLS ARE FOUND IN THE URINE.

10. Blood during the paroxysm.

Tendency to "coin-roll" formation less marked.

R. B. C. pale and often devoid of color.

Poikilocytosis.

If blood be withdrawn and allowed to clot, the serum which exudes will be red-tinted instead of straw colored as normally.

HEMOLYSIS.

DEFINITION.

The dissolution of the red cells with the passing out of its hemoglobin into the plasma or other medium in which the R. B. C. are suspended.

Hemolysis may be produced by certain **physical** agents: distilled water, freezing and thawing, temperature of 55° C. for 30 minutes.

It may also be brought about by certain **chemical** agents: most organic acids, mineral acids, all alkalies, bile salts, bichloride of mercury, etc.

Also by **animal venoms**: snakes, bees, spiders, etc.

Hemolysis by serum. This is quite different from hemolysis caused by the above forces.

The serum of one animal may be hemolytic to the red cells of another or several animals. **Its action depends upon the presence of two substances in the serum: amboceptor and complement**, both being mutually dependent upon each other in the process by which the red cells are destroyed. **IT FORMS THE BASIS OF THE SERUM DIAGNOSIS OF SYPHILIS.** (See p. 71.)

The red cells float in the plasma which has an osmotic pressure the same as that which exists within the red corpuscles. It is only when the osmotic pressure between plasma and corpuscles are disturbed that hemolysis can occur.

If red cells are suspended in a normal physiological salt solution (0.9% NaCl) which is isotonic with that of the blood, hemolysis will not occur.

COAGULATION OF THE BLOOD.

NORMAL COAGULATION TIME. (HEMATOPEXIS.)

Within 2 to 8 minutes after the blood leaves the blood vessel it clots or coagulates.

After 9 minutes, it is called delayed coagulation.

COAGULATION TIME IS DELAYED IN:

Anemia.	Scurvy,	Hemoglobinemia,
Jaundice,	Hemophilia,	Cobra bite.
Anasarca,	Asphyxia,	
Purpura,	Toxemias,	

COAGULATION OCCURS QUICKER IN:

Conditions associated with stasis.

Repeated hemorrhages.

Transfusions.

Hunger.

After using calcium chloride, coagulose, horse-serum, gelatin.

TESTS FOR COAGULATION TIME:

1. Several drops of blood are allowed to fall on a clean slide.

At intervals of one minute a broom straw or white horse hair (which has previously been boiled in alcohol and ether) is drawn lightly through each drop until a thread of fibrin is seen clinging to the straw or hair. This is a rough method.

2. Rudolph's Method. (Reader referred elsewhere). This is more accurate. The normal coagulation time with this method is $8\frac{1}{2}$ minutes.

Intravascular clotting.

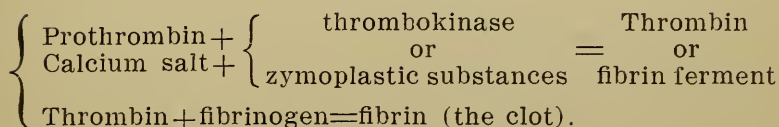
Blood never clots within a normal blood vessel under normal circumstances.

Intravascular clotting may be hastened by the introduction into the blood stream of foreign bodies or air which cause thrombi; or by injuring the endothelium of the arterial wall; by the injection of macerated lymph gland or horse serum, etc.

Methods of preventing extravascular clotting:

1. Freezing, which destroys the enzymes.
2. Drawing blood into concentrated magnesium sulphate solution. It combines with calcium.
3. Sodium oxalate (0.1% sol.). Combines with calcium.
4. Sodium fluoride.
5. Drawing blood into an oiled vessel and stirring with an oiled rod.

PHYSIOLOGY AND CHEMISTRY OF CLOTTING.



Explanation of these equations:

Prothrombin. Is inactive. Exists in the blood as a precursor of thrombin just as inactive trypsinogen is a precursor of trypsin.

Calcium salts. When absent clotting will not occur. It can readily be proven by adding ammonium oxalate to precipitate the calcium.

Thrombokinase. Derived from the tissues, the blood plates or the corpuscles and are the agency by which inactive prothrombin is converted into active thrombin in the presence of calcium salts.

Fibrinogen. A normal constituent of all blood plasma. This reacts with the newly formed thrombin and forms the clot which is called **fibrin**.

Fibrin (Clot). The clot is a network of fibrin in the plasma. In the meshes of the clot many red cells are entangled. The network is oftentimes seen to radiate from the blood plates.

When blood is first drawn into a vessel it becomes transformed into a semi-solid gelatinous mass. Later, the clot shrinks and a straw-colored liquid (plasma) collects at the top.

Plasma differs from serum in that it does not contain fibrinogen which was consumed during coagulation.

CHAPTER III.

EXAMINATION OF THE BLOOD FOR BACTERIA AND PARASITES.

TAKING BLOOD FROM A VEIN FOR CULTURE PURPOSES.

1. Ten c.c. of blood is withdrawn from the median basilic vein by means of a sterile Lürer syringe.
2. Transfer this blood immediately to an Erlenmeyer flask containing 150 c.c. broth (either plain or 1% glucose) and shake.
3. Incubate for 36 hours at a temperature of 37° C.
4. Shake, remove 15 c.c. and place into a centrifuge.
5. After 20 minutes centrifuging, decant the supernatant liquid and with the sediment inoculate agar slants.

TYPHOID FEVER.

1. The bacilli may be isolated from the blood even when a Widal reaction may not be positive.
2. Of the 10 c.c. blood taken for culture purposes, place 1 c.c. into each of 2 Erlenmeyer flasks containing 150 c.c. broth and into 2 more such flasks place 2 c.c. blood. We thus have 2 flasks with a dilution of 1:150 and 2 more with a dilution of 1:75.
3. Incubate for 24 to 36 hours.
4. Make a hanging drop examination for motile bacilli. If negative incubate for another 24 hours.
5. When the bouillon has become cloudy, make subcultures in milk and glucose bouillon and test again with an actively agglutinating serum.

Another method.

1. Add blood to sterilized ox bile in proportion of 1 c.c. blood to 5 c.c. ox bile.
2. Incubate 12 to 15 hours at 37° C.
3. Transfer a few loop fulls to either the Drigalski-Conradi or the Modified Endo Media.
4. The colonies which then develop are then subcultured and agglutination tests made.

With these media, positive agglutination tests are absolutely diagnostic of typhoid. No germs are found in the blood after the third week.

Widal Reaction. (See p. 69.)

PNEUMONIA.

1. The finding of the diplococcus of Fraenkel in the blood has more of a prognostic than diagnostic value.
2. Fraenkel claims that if 1 c.c. of the patient's blood be spread on agar plates and a luxuriant growth of colonies develop, we may infer that death from sepsis may occur or else metastasis to other organs may take place.
3. On the other hand, if the growth be small, and it becomes necessary to take larger volumes of blood to demonstrate the presence of diplococci and to grow them in bouillon instead of agar, the prognosis is much better.
4. The organisms can be demonstrated as early as 12 hours after the initial congestive chill.
5. The rule is that the diplococci disappear after the crisis.
6. Instead of using agar, Rosenow uses blood agar. The diplococci, when grown on blood agar plates produce greenish hemolytic zones. This distinguishes the pneumococcus from the streptococcus pyogenes which causes hemolysis without pigment production.
7. Rosenow also has a special stain to bring out the capsule of the pneumococcus.

ANTHRAX.

1. The bacilli are usually present in such large numbers that they may be found by simply making and staining a blood smear.
2. The stain consists of:
Concentrated sol. methylene blue..... 30 c.c.
Potassium hydrate sol. (1:10,000).....100 c.c.
3. Stain with this for 5 or 10 minutes.
4. Wash in 0.5% acetic acid sol. for 10 seconds.
5. Wash in alcohol and dry.

In doubtful cases, a guinea-pig should be injected with some of the patient's blood, and if anthrax be present a luxuriant growth takes place in this animal.

GONORRHEAL INFECTIONS.

1. Neisser's organisms may be found in the blood in cases associated with gonorrheal involvement of the endocardium, joints, etc.

SEPTICEMIA AND PYEMIA.

1. Streptococci may be found in the blood especially when the endocardium is involved.
2. These germs form typical chain-like growths.
3. In doubtful cases, one c.c. of venous blood should be injected intraperitoneally in a mouse. General septicemia will follow.

PUERPERAL INFECTION.

1. Blood cultures will show streptococci and staphylococci.
2. "Döderlein's cultures" from the uterus should also be made.

SCARLET FEVER.

1. Especially in severe and complicated cases streptococci may be found in the blood.

THE MALARIAL PARASITES.

PLASMODIUM VIVAX is associated with the tertian form of intermittent fever in which the paroxysms occur every 48 hours.

PLASMODIUM MALARIÆ is associated with the quartan form of intermittent fever in which the paroxysms occur every 72 hours.

PLASMODIUM FALCIPARUM is associated with estivo-autumnal fever. Duration of cycle segmentation **varies** from 24 to 72 hours.

Note.—The parasites are recognizable in both the unstained and in stained smears. For staining, the thionin, Nocht and Wright stains are preferred. The parasites are easily recognized in the unstained smears.

TERTIAN PARASITE UNSTAINED.

YOUNGEST (OR HYALINE) FORMS appear as
Small (2 microns), colorless, non-pigmented **disc**.

This shows an undulating rim of protoplasm, which encloses a single large nuclear body.

This body is surrounded by a "milky zone."

It is actively ameboid and changes its shape and position.

WHEN 12 HOURS OLD.

Ameboid motion very active so that pseudopodia may be seen which are very refractile.

Pigment now appears in the parasite.

They are light-brown granules with a rapid dancing motion.

These granules seem to be especially gathered in the ends of the pseudopodia.

Size: increases and also the R. B. C.

WHEN 24 HOURS OLD.

Size: fills about $\frac{1}{2}$ of the R. B. C.

Still actively ameboid.

Pigment increased.

Pigment is darker.

Less actively motile.

Scattered all over the parasite.

AT 40 HOURS THE PARASITE IS FULLY DEVELOPED.

Size: 8 to 10 microns.

Shape: round. Less distinct than the red cell.

Pigment: more abundant and evenly distributed.

The R. B. C. at this stage.

Is about $1\frac{1}{2}$ times its normal size.

Its outline can hardly be recognized.

PRESEGMENTAL STAGE.

Pigment: collects in the form of irregular clumps, the granules moving in irregular lines.

Outline: periphery of parasite slightly crenated and refractive dots appear on its border.

R. B. C.: disappears and the parasite becomes more dense and highly refractile.

SEGMENTAL STAGE.

Striations: from the crenated border radial lines appear in so-called "rosette" or "daisy-head" form. These radii are directed toward the center of the parasite and between these divisions we see highly refractile dots.

The segments become more and more distinct.

They finally separate into circular bodies having a central refractile dot.

Pigment: irregularly scattered between these segments. (Each segment is a hyaline form ready to attack another R. B. C.)

Besides the above-described intracellular hyalines, we occasionally find extracellular forms of the tertian parasite. There are two varieties.

(a) DEGENERATIVE FORMS.

These are extruded intracellulars which have died.

If it leaves the cell, the Hb. passes out of the cell, leaving a corpuscular shadow.

But this does not always occur, so that we usually find "dumbbell-shaped" organisms in the plasma.

During extrusion, the pigment is in active motion but ceases as the parasite dies.

Sometimes the parasite breaks up into fragments forming pigmented spherical bodies.

Or, they may be deformed and vacuolated—they are then called "sporulating forms."

(b) GAMETOCYTES.

Usually present in the blood a few days after the infection sets in.

There are 2 forms

1. Female or macrogamete.

2. Male or microgamete.

1. Female or macrogamete.

Three or four times the size of a red cell.

Pale, indistinct but actively ameboid.

Abundant pigment.

Some show no trace of the R. B. C.

Nucleus is $3\frac{1}{2}$ microns and is sometimes seen in the fresh specimen.

It is recognized by the fact that it is the only portion of the parasite which is not invaded by the pigment granules.

The female is formed from a **flagellum** of the parent cells, the **microgametocyte**.

The **microgametocyte** or parent cell is

Smaller than its offspring (female) being only 8 to 10 microns in diameter.

Its pigment is at first active. It soon forms a circle around the center and becomes motionless.

Sometimes it pushes out several **flagella** which are the **microgametes**.

2. Male or microgamete.

Two or 3 times the size of a R. B. C.

Often contains pigment granules.

These flagella break away from the parent cell, the latter then appearing as a small cell with central motionless pigment.

Flagellation does not occur in fresh specimens but occurs 15 to 20 minutes after the blood is drawn.

QUARTAN PARASITE UNSTAINED.

EARLY HYALINE FORMS cannot be differentiated from tertian but are easily recognized when **pigment** appears.

Pigment is coarser, darker in color, not so actively motile.

AS THE PARASITE GROWS—

Protoplasm: highly refractile.

Pseudopodia: very distinct.

Motility: less active.

R. B. C.: become smaller; margins crenated.

WHEN 24 HOURS OLD.

Shape: round or oval and very distinct.

Slightly ameboid.

Pigment: blackish-brown.

Peripheral location especially on one side.

Not motile at this stage.

(In the tertian the pigment is scattered all over.)

R. B. C.: very small, crenated, brassy in color.

AS IT CONTINUES TO GROW—

It becomes rounder and motility ceases.

Protoplasm very distinct and highly refractile.

Fills $\frac{1}{3}$ to $\frac{1}{2}$ of the R. B. C.

DURING THE THIRD DAY.

R. B. C.: Only a rim is left. The rim is dark and brassy.

The parasite is full grown (7 microns).

Pigment: travels from the periphery to the center in definite radial lines like the spokes of a wheel, the **pigment granules forming the spokes**. But the pigment soon collects in the center. This is the **presegmenter form**.

The parasite now becomes opaque and "rosette" demarcations appear. There are **6 to 12 segments**.

These segments are more perfect than the tertian, they become detached as hyaline forms and are ready to attack red cells again.

Gamete forms: Rarely seen here.

Resemble the tertian but usually smaller.

ESTIVO-AUTUMNAL PARASITE UNSTAINED.

HYALINE FORMS.

Resemble the other forms but slightly smaller.

Decidedly "signet-ring" in form and retain this appearance much longer.

(It differs from the tertian in that it causes the red cells to shrink.)

(It differs from the quartan by its smaller dimensions.)

Those rings which do not show the signet-ring appearance always present 2 nuclear bodies lying at opposite poles or close together.

AS THE PARASITE DEVELOPS.

Pigment: slight amount appears; usually motionless; located at periphery or at inner edge of the biconcavity.

Size: occupies $\frac{1}{5}$ of cell.

R. B. C.: exceedingly shrunken, crenated and brassy even in the early stages. The infected R. B. C.

now disappear from the peripheral circulation and migrate to the lymph glands, especially the spleen, there to continue its development.

Blood from a splenic puncture will show:

Pigment: greatly increased, coarser and darker, thus greatly resembling the quartan.

Size: parasite increased to 5 microns.

When full grown its pigment is in the center.

(Never diffuse as in the tertian.)

(More peripherally located than in the quartan.)

Rarely seen in peripheral circulation.

Segmentation. Similar to other forms.

Usually 15 very small segments.

SEVENTH DAY OF THE DISEASE (in the peripheral blood).

CRESCENTS AND OVOIDS APPEAR.

CRESCENTS.

Crescentic in shape with rounded ends.

Slightly longer than a R. B. C.

Very refractile.

Pigment in center.

Granules usually coarse and rod-shaped.

The crescents frequently change their shape to oval, dumbbell, circular and then resume the original form.

A small portion of the degenerated R. B. C. is attached to the crescent.

OVOIDS Have no corpuscular remnant.

Protoplasm not so refractile.

TERTIAN PARASITE STAINED.

YOUNG HYALINE FORMS of the parasite.

Protoplasm: ring-shaped, stained blue.

Achromatic area: a colorless "milky" area enclosed in the protoplasm.

Nucleus: a reddish-violet punctate spot at the thinnest portion of the ring which is shaped like a "signet-ring."

Size: 2 to 3 microns.

Location: in the center of a R. B. C.

Non-pigmented.

A PARASITE 24 HOURS OLD.

"Milky area" increases in size.

Chromatin dot begins to break up into groups of nuclei.

Pigment appears in the form of fine grains.

R. B. C. grow larger and paler.

MATURED OR FULL GROWN PARASITE.

Chromatin: completely broken up and diffusely scattered over the R. B. C. in the form of strands or masses.

These chromatin clumps divide into 15 to 20 dense round masses.

Around these masses protoplasm begins to collect.

In this stage, the protoplasm is devoid of color and it is always so in the segmenting cell.

Each of these chromatin clumps has a milky zone.

Pigment: greatly increased.

Size: at 48 hours the parasite occupies almost the entire swollen R. B. C.

Segmentation: occurs between 40 and 48 hours.

Pigment: collects centrally "en masse."

Protoplasm: divides in rosette or "daisy-head."

Note.—Some full-grown tertian parasites do not divide into segments.

These forms contain actively dancing pigment granules in the unstained specimen. (See p. 58.)

QUARTAN PARASITE STAINED. Resembles tertian parasites but

Chromatin mass is indistinct in the hyaline forms and in the older forms appears as an irregular clump of granules.

As it continues to grow, the parasite takes a form extending across the cell and occupies the major portion of the R. B. C. which has become shrunken and irregular in shape.

SEGMENT FORMS are more distinct.

- (a) They show more regular and geometric lines of cleavage with the chromatin exactly in the center of the crenated surface.

- (b) The pigment granules are coarser and much more distinct and more peripherally located.

Note.—Some full-grown parasites do not segment.

ESTIVO-AUTUMNAL PARASITE STAINED.

HYALINE FORMS.

Chromatin: appears as 2 or more dots or filaments.

Protoplasm: scantier than in the other forms. Thickening of the protoplasmic layer opposite the chromatin mass is very diagnostic.

GAMETE FORMS. Are distinctly spherical, being of the same thickness all the way round.

Nucleus forms a portion of the ring but does not project as in the asexual parasites. The R. B. C. in these sexual types do not show any coarse granular stippling.

CRESCENT FORMS. Very diagnostic of this form of malaria.

(a) Male crescent.

Chromatin: occupies the major portion of the cell. Appears as a loose net-work.

Protoplasm: little and stains blue.

Pigment: universally scattered throughout its body.

Shape: somewhat kidney-shaped and shorter and broader than the female.

(b) Female crescent.

Size: larger and narrower than male.

Chromatin: compact and centrally located.

Pigment: in a ring around the nucleus or in a clump at the center.

Protoplasm: abundant and bluish in color.

CIRCULAR FORMS. Two types are present:

1. Microgametocyte.

Size: smaller than a R. B. C.

Shape: distinctly spherical.

Chromatin: in center in a large irregular mass or in several dense masses near the periphery.

These masses containing chromatin are later extruded and form the flagella or microgametes.

2. Macrogametocyte.

Size: 2 or 3 times the former.

Shape: often triangular.

Protoplasm: abundant and blue-staining.

Chromatin: in a single mass at the periphery and is surrounded by a circle of pigment.

THE MALARIAL FEVERS.

1. For description of the parasites, see pages 57 to 64.
2. Enormous reduction in the number of R. B. C. occurs in acute attacks. A count of one million may be obtained on the first day.
3. In chronic cases we find features of a secondary anemia.

Polychromatophilia and granular degeneration of the R. B. C. progress steadily.

The estivo-autumnal parasite may create a blood picture closely resembling that of pernicious anemia.

The quartan and estivo-autumnal parasites cause a shrinking of the R. B. C. and these cells assume a brassy tone.

4. Absence of leucocytosis. But, relative lymphocytosis just as in typhoid.
5. In the afebrile period and sometimes throughout the disease eosinophilia occurs.
6. Pigmented leucocytes very common. (Phagocytes.)

RELAPSING FEVER.

1. In fresh blood, actively motile, cork-screw organisms are readily seen.
2. A dried smear stained with fuchsin or the aniline dyes depicts the *Spirochetæ* of Obermeier plainly.
3. The spirilli can only be found during the febrile paroxysm. In the fresh specimen it is seen to move slowly among the R. B. C. but does not molest them.
4. With each successive paroxysm the spirilli increase in number.

5. A leucocytosis is very characteristic of this disease, especially just after the crisis. The disease is also called "Seven-day Fever."

TRYPANOSOMIASIS. (SLEEPING SICKNESS.)

1. A nucleated, fusiform, flagellated parasite, the **trypanosoma Gambiense**, having an undulating membrane may be seen in the blood but never within the corpuscles.
2. The parasites vary greatly in number from day to day.
3. Best stained with the polychrome dyes. They show—
 - (a) nucleus, which is large and red.
 - (b) Centersome, intensely stained and located in a vacuole-like area near the blunt end.
 - (c) Line of chromatin running down the edge of the undulating membrane and terminating in the flagellum. The chromatic line and flagellum are both stained red.
 - (d) Protoplasm of the body is distinctly blue.
4. In genuine cases, the parasites should be found in the cerebro-spinal fluid.

FILARIASIS.

1. The **filaria sanguinis hominis** (Bancrofti) are seen under the microscope in active motion. However, they lose their motility very quickly.
2. The embryo is surrounded by a sheath which is considerably larger than the parasite and shows fine cross striations.
3. They are about the thickness of a red cell and about 1/90th of an inch long.
4. All examinations must be made at night, their numbers gradually rising to a maximum about midnight.
5. Only the **embryos** are found in the blood; the adult forms remaining in the lymphatics where they obstruct the flow of lymph and cause lymph-scrotum, hematochyluria, etc.
6. A thick blood smear is essential.
7. Eosinophilia is very characteristic.

SYPHILIS.

1. The *spirochæte pallida* can be demonstrated in both peripheral blood and in the blood from a splenic puncture and in certain skin lesions when a **dark field illuminator** is used.
2. Best stained with **Goldhorn's stain**.

Technic.

1. Fix smear with pure methyl alcohol for 15 minutes.
 2. Flood with polychrome methylene blue 3 to 5 seconds.
 3. Drain the excess off.
 4. Place slide slowly in clean water (film side down) and keep in this position 5 seconds.
 5. Shake in water to remove excess of the dye. The *spirochæte* appear violet colored.
 6. By staining with Gram's iodine solution for 15 to 20 seconds, washed and dried, and examined with oil-immersion lens, the organisms give up their violet color and become bluish-black.
3. Other good stains are: Giemsa's and Levaditi's.

ROCKY MOUNTAIN SPOTTED FEVER. (Tick fever.)

1. The parasite, the *piroplasma hominis* attacks the red cells.
2. Three forms of this intracellular ovoid parasites occur.
3. Best stained with polychrome dyes.

TEST FOR PUS IN THE BLOOD. (IODOPHILIC REACTION.)

1. A dried unfixed blood smear is first exposed to the vapors of solid iodine until it assumes a brownish color.
2. Then mount with this titration:

Iodine.....	1 G.
Potassium iodide.....	3 G.
Dist. water.....	100 c.c.

To which a sufficient amount of gum arabic is added to make a syrup (a brownish, ropy fluid).
3. One drop of this titration is sufficient. The cover slip should be pressed tightly.
4. After 15 minutes examine with oil-immersion lens.

Positive reaction.

Brown or mahogany colored granules within the polymorphonuclear leucocytes. The protoplasm may also at times show a diffuse brown stain.

Although the reaction is usually confined to the neutrophils, the mononuclear cells may also be tinged brown.

This so-called intracellular reaction is more important than the extracellular reaction in the blood plates.

Negative reaction.

In the absence of pus, the protoplasm of the leucocytes are stained bright yellow and the nuclei are much lighter.

BREMER'S BLOOD TEST IN DIABETES.

1. A thick fresh blood smear is fixed by dry heat and allowed to cool.
2. Then flood with a 1% aqueous solution of congo-red for a few minutes.
3. Wash in water.

Normal blood: stains bright red.

Diabetic blood: either refuses to stain or else takes on a faint yellowish or greenish hue.

May be obtained before glycosuria becomes marked.

A positive reaction may occur in other diseases, e. g., leukemia, goitre, Hodgkin's disease, etc., hence it is not a specific test.

Note.—A 1% solution of Biebrich Scarlet will stain diabetic blood intensely, whereas normal blood does not take up the stain.

In diabetes, the blood shows lipemia. Extracellular fat globules are seen.

WILLIAMSON'S TEST IN DIABETES.

1. Dissolve 2 drops of blood in 4 drops of water.
2. Then add 1 c.c. of a 1:6,000 aqueous solution of methylene blue.
3. To this add 4 drops of a 6% solution of liquor potassæ.
4. The test should be performed in a test tube. At this point place the test tube in boiling water for 4 minutes.

Normal blood: color remains deep blue.

Diabetic blood: decolorizes the solution.

Diabetic urine: gives same reaction.

Note.—Do not use more blood than what is stated above because decolorization will occur with larger quantities.

GRÜBER-WIDAL REACTION IN TYPHOID.

THE "HANGING-DROP" OR MICROSCOPIC METHOD.

1. With a special capillary pipette with a central bulbar enlargement, draw up 15 to 20 drops of blood from a pricked ear.
2. Lay the pipette flat until coagulation occurs. The serum which exudes is preferable to whole blood.
3. Serum may also be obtained by using cantharides so as to cause a blister.
4. Dilute this serum with physiological salt solution (performing this on watch crystal) so as to make one dilution of 1:25 and another one of 1:50. (This means one drop of serum and 24 and 49 drops of salt solution.)
5. Take one platinum loop full of each dilution and mix with one loop of a standard suspension of typhoid germs. The dilutions are now 1:50 and 1:100. These typhoid suspensions must be fresh and the germs must be actively motile. Strains which have passed through several generations on artificial media are the best.
6. From the above last 2 dilutions, hanging-drop preparations should be made and examined.

Reaction. With a dilution of 1:50, and within a period of one hour, a marked clumping together and complete loss of motility of these typhoid germs signifies a positive reaction. **THE TIME and DILUTION ARE VERY IMPORTANT.**

MACROSCOPIC METHODS. Cultures which have been killed by heat, formalin, carbolic, etc., are employed. Clumps of bacilli settle to the bottom of the test tube leaving a clear supernatant liquid. **Ficker's Typhus Diagnostikum** very good. It is sold by Merck & Co.

BASS AND WATKIN'S MODIFICATION OF THE MACROSCOPIC METHOD.

1. Mix a full drop of blood serum with 4 drops water.
2. Add 4 drops of the following suspension to the above. (10,000 million killed typhoid germs per c.c. in 1.7% NaCl to which 1% formaline is added.)
3. Tilt slide from side to side so as to keep the mixture flowing back and forth.

Positive reaction. Grayish, mealy sediment within one minute. This sediment appears in the fluid and around the edges and tends to collect there. If the agitation be continued, the clumps increase in size for 2 or 3 minutes.

Negative reaction. Absence of agglutination of the mixture. It remains clear. If the reaction fails to appear within 2 or 3 minutes it will not appear at all.

Advantage. Can be quickly performed at bedside.
Reliability.

BLOOD TESTS FOR SYPHILIS.

1. JUSTUS'S TEST.

A rapid reduction in the percentage hemoglobin (10 to 20%) follows mercurial treatment (inunction or injection) in florid syphilitic patients. It lasts from a few hours to a few days.

Objection. Mercury salts alone may cause an anemia in consequence of their hemolytic action upon the red blood corpuscles.

2. SERUM COLOR REACTIONS.

1. To 0.1 c.c. serum add enough physiological salt solution to bring the quantity up to 3 or 4 c.c.
2. Then add 1 drop perhydrol (as an oxidizer).
3. Mix this with 0.5 c.c. of Schürman's reagent (prepared fresh):

Carbolic acid.....	0.5
5% aqueous solution ferric chloride.....	0.62
Distilled water.....	34.5

Positive reaction. As the reagent is allowed to trickle down the test tube, a dark brown color will be observed at the junction of the fluids. On shaking, the mixture appears very thick. To be of value, the reaction must occur within 1 or 2 minutes.

Normal blood serum. A slight green ring occurs at the junction of the liquids. But, it disappears almost entirely on shaking. The mixture also remains clear and transparent.

Note.—Landau's serum color reaction is now in its experimental stage. Reports thus far do not affirm its specificity for syphilis.

3. WASSERMANN'S REACTION.

1. The Wassermann test or any of its modifications, when positive, is a specific test for lues.

A negative reaction does not rule out syphilis.

Repeated examinations are necessary.

2. The Noguchi modification is superior to the Wassermann test because the percentage of positive results is somewhat higher.
3. Under vigorous mercurial treatment and with "606" a positive test once obtained may disappear, but it does not mean that the patient is cured.
4. All tests are based on the Bordet-Gengou phenomenon of complement fixation to determine the presence of the syphilitic antibody in the patient's blood serum. The tests are interpreted according to the degree of hemolysis visible in the test tubes.

THE A-B-C OF THE SERUM DIAGNOSIS OF SYPHILIS.

DEFINITION OF TERMS.

HEMOLYSIS. Dissolution of the red blood corpuscles and the passing out of the red coloring matter (hemoglobin) into any medium in which the erythrocytes may be suspended.

Hemolytic substances are those substances capable of producing hemolysis. (See page 51.)

Fresh blood of many animals is hemolytic for the R. B. C. of some, but not all, other species.

Hemolysis depends upon three factors:

1. Amboceptor.

Amboceptor cannot act without complement.

2. Complement.

Complement cannot act without amboceptor.

3. Corpuscles.

Both combined must act on the R. B. C.

COMPLEMENT.

1. It is one of the factors necessary for hemolysis.
2. It is always present in fresh sera.
3. It is destroyed by heating for one-half hour at 55° C. Serum thus heated becomes **inactivated**.
4. If the serum be taken from a guinea-pig, it is called guinea-pig complement.

Inactivation. Depriving fresh serum of its complement.

Reactivation.

1. When fresh serum is added to an inactivated serum the latter again becomes activated.
2. Complement can always reactivate the serum of the same species from which it is derived.

But, not every complement can activate the sera of other species. However, **guinea-pig** complement is characterized by its remarkable ability to reactivate sera of **alien** species. It is, therefore, used whenever it becomes necessary to substitute the complement of one serum for that of another which has become inactivated or has deteriorated.

AMBOCEPTOR OR HEMOLYSIN.

1. The serum of the blood of an animal which has been immunized with R. B. C. of another species gives us amboceptor. The injected animal develops in its serum anti-bodies.
2. It is one of the three factors necessary for the production of hemolysis.
3. It is stable; not being destroyed by heating as is the case with complement.
4. Amboceptors are **specific**. They can act upon the R. B. C. of one animal only. The prefix "anti" is usually added to the name of the species which has been used to bring about the immunization.
5. **Some** sera contain **several** kinds of amboceptors. Thus one particular serum may have amboceptors for sheep, for rabbits, for dogs, etc.
6. **Natural amboceptors.** Are those amboceptors already existing in the serum of a given animal.

7. **Immune amboceptors.** By repeatedly injecting an animal with R. B. C. of another alien animal, we may create specific amboceptors for this animal, or, we may increase the amount of natural amboceptor already present.

When red blood cells are injected, the amboceptors created are also designated as **hemolytic amboceptors** for the purpose of contrasting to **bacteriolytic amboceptors** which are produced when bacteria are injected into an animal. The dissolution of the bacteria (whereas in the other case it is the corpuscles) is known as bacteriolysis as compared to hemolysis.

After immunization, the serum of the immunized animal gradually loses its hemolytic power, but may be rapidly increased by a few injections of the red cells first used in the process of immunization.

ANTIGENS.

1. A general term applied to a group of substances capable of producing specific antibodies (when injected into a suitable animal). Diphtheria toxin is an antigen because injections thereof are followed by the appearance of a specific antitoxin in the horse. Red blood cells and bacteria may also act as antigens.
2. These **antibodies** are specific for the substances from whence they are derived. Given a known antibody we can determine the unknown antigen owing to this specificity.

COMPLEMENT FIXATION.

1. A disappearance of the complement in a mixture of antigen and antibody.
2. A distinct relation exists between the combination of antigen and antibody with that of complement.

The R. B. C. (as antigen) acted upon by amboceptor (antibody) becomes so altered as to absorb the complement and undergo hemolysis.

In the same way, bacteria as antigen, having been acted upon by amboceptor (antibody), take up the complement and become dissolved.

3. Sera of various animals show marked differences in their power of complement fixation.

4. Whereas a given serum might possess the property of reactivating the hemolytic amboceptor of an inactivated serum, this same serum of the given species may possess little or no fixation property. This fact is very useful in diagnosis.

Guinea-pig's complement is very readily fixed.

Rabbit's complement possesses the best reactivating property for the rabbit's amboceptor.

5. By means of the complement fixation reaction, antigen may be detected **indirectly**. Antigen may also be detected **directly** because of the specificity of antibody and antigen.
6. Five factors enter into the complement fixation reaction in the diagnosis of syphilis.
 - i. **Red blood cells.**
 - ii. **Hemolytic amboceptor.**
 - iii. **Complement.**

These three are collectively designated as the "**hemolytic system.**"

- iv. **Syphilitic antigen** or extract of syphilitic liver.

Whereas the R. B. C. are also antigens, we do not refer to these antigens when the term antigen is used, but to syphilitic antigen.

- v. **Antibody.** Whereas hemolytic amboceptor is also an antibody, antigen as used in the test, refers to antibody present or absent in the serum under investigation for syphilis.

ANTI-COMPLEMENTARY SUBSTANCES AND ANTI-COMPLEMENTARY ACTION.

Substances possessing the power of **reducing** or **totally removing** the action of the complement are designated as anti-complementary.

Most acids, alkalies and certain salts have such action.

Such substances may also be present in certain sera. Human serum gradually acquires this property on standing. Repeated injections of fresh serum into an animal of another species causes the production of such substances. (Ehrlich and Morgenroth). Bacterial infection may cause the serum to become anti-complementary but it is said that heating to 56° C. for 30 minutes rids the serum of this difficulty.

BASIS OF THE WASSERMANN REACTION AND ITS MODIFICATIONS.

The complement, which is essential for the production of hemolysis (dissolution of the red cells) is **fixed** so that it cannot take part in this process. The result is that no hemolysis can take place. Inhibition of hemolysis is not necessarily complete. Our conclusions are based upon the degree or extent of the inhibition of hemolysis. The results are expressed in percentages or by a variable number of **plus (+)** signs.

1. The Original Wassermann Test.

1. **ANTIGEN.** A watery extract is used in the original test.

- (a) The liver or spleen of a congenitally syphilitic fetus is cut up into small pieces and minced in a meat grinder.
- (b) For every part of tissue add 4 parts normal salt solution to which carbolic acid is added in the proportion of 0.5%.
- (c) Shake the mixture well in a dark bottle for 24 hours by means of a shaking machine.
- (d) Centrifuge. The brownish opalescent supernatant liquid is antigen. It must be preserved in a rubber-stoppered brown bottle in a refrigerator.

On standing, a precipitate sediments. This should neither be used nor disturbed. When in need of antigen, decant the required amount of antigen and replace balance in refrigerator. Do not expose to light.

- (e) Titration of antigen.

Use 0.8, 0.6, 0.4 and 0.2 c.c. of the extract in the presence of 1 c.c. complement, twice the hemolytic dose of the amboceptor and 1 c.c. of 5% sheep's corpuscles for its anti-complementary properties, and in the same quantities **plus** 1 c.c. of 5% sheep's cells for its hemolytic qualities.

If the antigen be not hemolytic in 0.4 and not anti-complementary in 0.4 according to the rule of Weil and Nakayama, this antigen will be employed in one-half of 0.4 c.c. (equals 0.2 c.c.).

2. PATIENT'S SERUM.

Blood is obtained from a vein. It is permitted to clot and the serum is collected.

Serum is inactivated by heating to 56° C. for 30 minutes.

Inactivation must be performed within 12 hours. The native complement is thus destroyed.

If cerebro-spinal fluid be employed, do not inactivate.

The test doses are 0.1 and 0.2 c.c.

3. COMPLEMENT.

One c.c. of guinea-pig's serum in 1:10 dilution. It must not be older than 12 hours.

4. AMBOCEPTOR.

Rabbits are immunized against sheep's R. B. C. by intraperitoneal injections. One unit of amboceptor should be determined by titrating against 1 c.c. of 5% suspension of washed R. B. C. of sheep, using 0.5 c.c. of the above diluted complement. In the actual test use 2 units.

5. CORPUSCLE SUSPENSION.

One c.c. of a 5% suspension of washed sheep's corpuscles. Should be kept on ice and not older than 24 hours.

Sheep blood is drawn into a sterile wide-mouthed bottle, in which are a number of glass beads, and vigorously shaken immediately so as to defibrinate the blood and prevent clotting.

RESULTS SHOULD BE

The degree of hemolysis in these first 2 tubes determines the nature of the serum.
 Complete Hemolysis
 Complete Hemolysis
 Complete Hemolysis
 Complete Hemolysis

No Hemolysis
 No Hemolysis
 Complete Hemolysis
 Complete Hemolysis
 Complete Hemolysis
 Complete Hemolysis

Complete Hemolysis
 Complete Hemolysis
 Complete Hemolysis
 Complete Hemolysis
 Complete Hemolysis
 Complete Hemolysis

Complete Hemolysis
 Complete Hemolysis
 Complete Hemolysis
 Complete Hemolysis
 Complete Hemolysis
 No Hemolysis

The volume of each tube is now 5 c. c. Mix the contents of tubes thoroughly and incubate at 37° C. for 2 hours. Then remove tubes to refrigerator and keep there over night.

IMMUNE ANTI-SHEEP AMBOCEPTOR (TITER 1:2000) 1:1000 DILUTION.

5% SUSPENSION OF WASHED SHEEP'S CORPUSCLES.

The volume of each tube is now brought up to 3 c. c. with Salt Solution and incubate for 1 hour at 37° C.

GUINEA-PIG COMPLEMENT IN 1:10 DILUTION.

WATERY EXTRACT OF NORMAL LIVER.

WATERY EXTRACT OF SYPHILITIC LIVER (AS ANTI-GEN).

PATIENT'S SERUM (56° C.)

1 0.2
 2 0.1
 3 0.2
 4 0.1
 5 0.4
 6 0.6

POSITIVELY SYPHILITIC SERUM (56° C.)

7 0.2
 8 0.1
 9 0.2
 10 0.1
 11 0.4
 12 0.6

NORMAL SERUM (56° C.)

13 0.2
 14 0.1
 15 0.2
 16 0.1
 17 0.4
 18 0.6

CONTROLS

19 No Serum
 20 No Serum
 21 No Serum
 22 No Serum
 23 No Serum
 24 No Serum
 25 No Serum

THE WASSERMANN SYSTEM (Citron).

All numbers in this table excepting the consecutive numbers from 1 to 25 signify cubic centimeters. There are 25 test tubes used.

WASSERMANN TEST WITH SIX TUBES.

1. Arrange 6 tubes in pairs as shown under the discussion of the Noguchi modification on page 83.
2. In No. 1 and No. 2, place 0.2 c.c. of the inactivated serum of a known syphilitic.
3. In No. 3 and No. 4, place 0.2 c.c. of the inactivated serum from the patient in question.
4. In No. 5 and No. 6, place 0.2 c.c. of the inactivated serum of a known normal person.
5. To all of the tubes add 0.1 c.c. of fresh guinea-pig complement.
6. To the tubes in the front row (Nos. 1, 3 and 5), add one unit antigen.
7. To all of the tubes add 3 c.c. normal salt solution.
8. Shake all tubes vigorously.
9. Incubate at 37° C. for one hour and then remove.
10. To all of the tubes add 2 units of amboceptor and 1 c.c. of the suspension of sheep's red blood corpuscles.
11. Incubate 2 hours.
12. Remove and then place on ice 20 hours.

REACTION. Hemolysis should be complete in the rear row of tubes and in the tube No. 5 in the front row containing normal serum.

Complete inhibition in No. 1.

No. 3, containing the patient's serum, will show inhibition of hemolysis of various intensities if the patient be infected with syphilis.

DEDUCTIONS FROM THE WASSERMANN TEST.

Note.—The syphilitic antibody present in the patient's serum may vary in amount, hence the complement may be fixed to a variable degree. When complement is fixed, it can no longer act in conjunction with amboceptor in that process known as hemolysis. In other words, hemolysis is inhibited in varying degrees depending upon the amount of syphilitic antibody present.

- (a) If complete inhibition of hemolysis be present in the tube containing 0.1 c.c. serum and 0.1 c.c. antigen, the result is expressed by Citron thus:
++++.

- (b) If not complete in the tube containing 0.1 c.c. but complete in the tube containing 0.2 c.c., the result is expressed thus: $+++$.

The results in (a) and (b) are called **STRONGLY POSITIVE**.

- (c) If hemolysis be complete in tube containing 0.1 c.c. serum while that containing 0.2 c.c. shows complete inhibition, the result is expressed thus: $++$.

- (d) Incomplete inhibition in the tube containing 0.2 c.c. is expressed thus: $+$.

The results in (c) and (d) are called **WEAKLY POSITIVE**.

- (e) When inhibition in the tube containing 0.2 c.c. is doubtful, the result is expressed thus: $\pm$.

2. Noguchi Modification.

It has been found that human serum contains a variable amount of **natural** sheep amboceptor. For this reason, Noguchi employs an anti-human hemolytic system to replace the anti-sheep hemolytic system of the original Wassermann.

Five factors enter into the Noguchi modification (as in all others):—

1. ANTI-HUMAN HEMOLYTIC AMBOCEPTOR.

Rabbits are immunized with human R. B. C.

Preparation.

Rabbits are injected (intraperitoneally) with increasing doses of washed human R. B. C. allowing 5 days to elapse between each injection.

1st injection..... 5 c.c. washed human R. B. C.

2nd injection..... 8 c.c. washed human R. B. C.

3rd injection..... 12 c.c. washed human R. B. C.

4th injection..... 15 c.c. washed human R. B. C.

5th injection..... 20 c.c. washed human R. B. C.

The serum is collected from the immunized animal 9 or 10 days after the last injection by bleeding the rabbit (from carotid artery).

[The corpuscles must be washed at least 3 times with large amount of saline solution (0.9%).]

Having collected the blood, allow same to stand at room temperature for several hours during which time coagulation occurs. If the clot does not contract within 4 or 5 hours and remains adherent to the sides of the tube, insert a platinum needle (sterile) between the clot and the walls of the tube and detach the clot. Allow this to remain 4 or 5 hours again at room temperature.

Now place in refrigerator for 24 hours. Centrifuge.

Decant supernatant serum. For about 3 days after, some more serum will exude and this can be also utilized. These daily sera may be mixed together.

If the serum be not clear, it may be clarified by centrifugalization or by permitting the tube to stand—when sedimentation occurs and then decanting.

Amboceptor must be titrated. The titre of the serum is expressed by the smallest amount of serum which is found to be necessary for complete dissolution of a fixed amount of red blood corpuscles and a fixed amount of complement.

A good preparation will have the value of one unit in something less than 0.001 c.c. of serum, that is, 0.001 of serum or less, will cause complete hemolysis of 1 c.c. of a 1% suspension of human R. B. C. when combined with 0.02 c.c. of guinea-pig's fresh serum (0.1 c.c. of 20% dilution).

2. PATIENT'S SERUM TO BE TESTED.

With a Hagedorn needle puncture the skin over the last joint of the middle finger (ventral aspect).

Collect the exuding drops in a Wright's blood capsule through the curved end of same.

Seal the straight capillary end by a flame and shake the blood down into this end after the capsule has cooled.

Then seal the other end.

The blood clots in the capsule and serum exudes.

When ready for the test break the capsule.

3. HUMAN CORPUSCLE SUSPENSION.

Into a 10 c.c. graduated centrifuge tube place 9 c.c. of the following citrate solution.

Sodium citrate..... 20 G.
Normal salt sol. (0.9%).....1000 c.c.

Permit the blood of a normal person to drop into this mixture until the volume in the tube registers 10 c.c. Mix well and centrifuge.

Pour off the supernatant liquid and fill tube again with salt solution.

Mix again, centrifuge, and again decant supernatant fluid leaving a deposit containing corpuscles freed from serum.

Now resuspend the corpuscles in salt solution. To make a 1% suspension, add 100 c.c. salt solution. To make a 10% suspension, add 10 c.c. salt solution.

We may use these standard suspensions in the proportion of 1 c.c. of the 1% solution or 0.1 c.c. of the 10% solution. The latter one is preferred.

4. GUINEA-PIG'S SERUM AS COMPLEMENT.

Bleed the normal guinea-pig at the carotid artery, allowing blood to flow into large Petri dish.

Cover dish and allow to stand at room temperature for a few hours when coagulation will have occurred and serum exuded.

To complete the separation of the serum, the dish may be placed in a refrigerator.

After 5 to 10 hours decant the serum into a test tube and keep in a refrigerator when not in use.

Since complement deteriorates in 24 hours, blood may be aspirated directly from the guinea-pig's heart.

The dilution used is 40%. One c.c. of complement is mixed with $1\frac{1}{2}$ c.c. of physiological salt solution.

(The guinea-pig will stand the loss of 5 to 10 c.c. blood but don't puncture again until after 28 days have elapsed.)

5. ANTIGEN. (Preparation.)

Extract a mashed paste of liver, heart or kidney of man, ox, guinea-pig, rabbit or dog with

Ten parts absolute alcohol at 37° C. for several days.

Filter through filter paper and collect the filtrate.

Allow the filtrate to evaporate to dryness with the assistance of an electric fan.

Take up the dried residue with ether and permit the turbid solution to stand in a covered dish in a cool place over night. In the morning, the turbidity will have disappeared.

Decant the clear etherial solution into a clean beaker and concentrate by evaporating most of the ether.

Mix this concentrated solution with 10 volumes of pure acetone.

Allow precipitate to settle and decant supernatant fluid.

This antigen is a slightly brownish precipitate which gradually becomes sticky on exposure to air.

This acetone-insoluble portion of the tissue extract containing antigenic lipoids must be examined for its quality and strength and more especially with regard to its hemolytic and anti-complementary actions.

By **anti-complementary action**, we mean a diminution or a destruction of the activity of the complement. To make a **stock solution**:

3/10 G. of this acetone-insoluble fraction is dissolved in 1 c.c. ether and mixed with 9 c.c. methyl alcohol.

If any precipitate forms or is left undissolved, remove by centrifugation.

The stock solution contains 3% of lipoids from which an emulsion can be made when ready for it.

The **emulsion** is made by mixing

1 c.c. of the stock solution with
9 c.c. physiological salt solution.

This produces a clear opalescent solution containing 0.3% of the original lipoids. We only use 1/10 c.c. of this emulsion in the test.

The **antigenic** property of the extract must be determined, that is, its power of production of complement fixation in the presence of syphilitic serum.

1. **Test for hemolytic action of antigen.**

Antigen emulsion.....	0.4 c.c.
Salt solution.....	0.6 c.c.
10% corpuscle suspension.....	0.1 c.c.

Incubate at 37° C. for 2 hours.

2. Test for anti-complementary action of antigen.

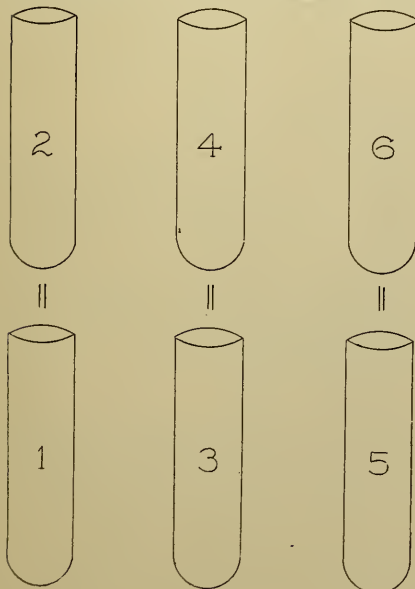
Antigen emulsion.....	0.4 c.c.
Salt solution.....	0.6 c.c.
40% complement.....	0.1 c.c.
Amboceptor.	2 units
Incubate at 37° C. for 1 hour.	
Corpuscle suspension 10%.....	0.1 c.c.
Incubate at 37° C. for 2 hours.	

3. Test for antigenic property.

Antigen emulsion (1:10).....	0.2 c.c.
Salt solution	0.8
Syphilitic serum	0.02
(1 drop from a capillary pipette)	
40% complement.....	0.1
Amboceptor.	2 units
Incubate at 37° C. for 1 hour.	
10% corpuscle suspension.....	0.1 c.c.
Incubate at 37° C. for 2 hours.	

Noguchi claims that at least 4 antigen doses must be used. To obtain this he recommends the use of a 0.1 c.c. of a 0.3% suspension of acetone-insoluble tissue lipoids. In this quantity there will be at least 5 antigen doses ($0.1 \text{ c.c.} \div 0.02 \text{ c.c.} = 5$).

TECHNIC (of the Noguchi modification).



Arrange 6 test-tubes in pairs as shown in the illustration.

Into No. 1 and No. 2 place one drop (0.2 c.c.) (from a capillary pipette) of the patient's serum to be tested.

Into No. 3 and No. 4 (which are to serve as **positive controls**) place one drop of the serum of a person known to be syphilitic or who have given a positive reaction.

Into No. 5 and No. 6 place one drop of the serum of a normal individual. These are called **negative controls**.

To each of the 6 tubes add 1 c.c. of the suspension of washed human corpuscles and 0.04 c.c. fresh guinea-pig serum as complement.

To tubes 1, 3 and 5, add one drop of the antigen solution.

Shake all tubes vigorously and incubate for 1 hour at a temperature of 37° C.

Then add 2 units of anti-human amboceptor to each of the six tubes and shake well.

Incubate all the tubes at 37° C. for 1 hour more.

Remove from incubator and permit to stand at room temperature for the next 10 or 12 hours during which time the reaction may be watched as it progresses and read.

Deductions. The 3 even-numbered tubes should show complete hemolysis. The color should be uniformly red but no corpuscular sediment.

Tube No. 5 should show complete hemolysis before the final reading is made.

Tube No. 3 will be clear.

Tube No. 1: if it resembles No. 3, reaction is positive; if it resembles Nos. 2, 4 or 6, reaction is negative.

3. Method of Cyrus W. Field.

He employs **cholesterinized antigen**. The velocity of the test seems to be increased thereby. Each c.c. of the diluted antigen contains 0.1 mg. of the combined lipoids and cholesterin. It is easily prepared and is rarely, if ever, anti-complementary or hemolytic as are the Wassermann and Noguchi antigens. The essential point in this method is the **standardization of antigen**, which means that irrespective where the test is made, whether in New York, San Francisco or New Orleans, the results will always be the same.

Antigen. Alcoholic extract of a large number of guinea-pig's hearts with one-half saturation with cholesterin. 20 c.c. of this cholesterinized extract is evaporated and dessicated and the residue weighed.

The extract is then used in such dilution that 1 c.c. thereof represents 1 mgm. of the cholesterin lipoids.

CORRECTION.

Transpose line 9 which reads "Add the antigen, complement (which is usually 0.5" immediately before line 14. It will then read:—

Add the antigen, complement (which is usually 0.5 c.c. of a 1:8 dilution) to the serum and incubate for 40 to 50 minutes at 37° C.

Anti-sheep hemolytic amboceptor.

Complement in the dilution of 1:8. At least 2 units of amboceptor and $2\frac{1}{2}$ units of complement should be used.

Technic:

Racks holding 8 tubes are set up. Label consecutively from 1 to 8.

Into each of 7 tubes place 0.1 c.c. of the patient's serum.

Add the antigen, complement (which is usually 0.5

Into the 8th tube place twice that amount (0.2). (Tubes No. 1 and No. 8 are used as controls.)

To the other 6 tubes add antigen in the following amounts: (expressed in c.c.) 1, 0.8, 0.6, 0.4, 0.2 and 0.09. c.c. of a 1:8 dilution) to the serum and incubate for 40 to 50 minutes at 37° C.

Mix the amboceptor and the suspension of R. B. C. in their proper proportions and add sufficient salt solution so that each c.c. of the mixture represents at least 2 units of amboceptor and 0.5 c.c. erythrocytes. The mixture is incubated at least 30 minutes before being mixed with the serum-antigen-complement mixture.

The results are read off as soon as the 2 control tubes show complete hemolysis and labeled according to the following scheme:

0. Represents complete hemolysis, while
1. Slight inhibition of hemolysis, while
2. Marked inhibition of hemolysis, while
3. Complete inhibition of hemolysis.

SERO-DIAGNOSIS OF PREGNANCY.

Abderhalden's Test.

The **DIALYZATION METHOD** is preferred to the Optic Method.

The **basis** of the test consists in the conversion of colloidal non-dialyzable placental proteid into dialyzable products through the activity of certain ferments.

These products may then be detected by simple color reactions in the dialysate.

THINGS NECESSARY FOR THE TEST.

1. Fresh coagulated placental proteid (albumin).
2. **Blood.** Ten c.c. venous blood from suspected female is centrifuged. Serum is drawn off into a clean sterile tube.

Note.—Since the amino acids which form during digestion may give a positive reaction with triketohydrinden hydrate, all blood specimens should be taken before breakfast.

3. **Dialyzing tubes.** The dialyzing thimbles must be permeable for peptones but not for albumin.

TECHNIC.

1. Into each of 3 thimbles place 1 G. of coagulated placental proteid (albumin) which has been washed in distilled water, dried between filter paper and ground up in a mortar.
2. To thimble No. 1, add 2 or 3 c.c. of hemoglobin-free serum to be tested. Overlay this mixture with toluol.
3. Place thimble, et al., in a sterile dialyzing tube containing 20 c.c. distilled water which should stand slightly higher than the fluid in the thimble.
4. Overlay the external fluids with toluol and plug the dialyzing vessel with cotton to hold in place the thread which suspends the shell.
5. Incubate at 37° C. for 18 hours. Then test the dialysate for peptone.
6. **Thimbles number 2 and 3 are controls.**

In Thimble No. 2. Place 1 G placental albumin and 2 c.c. of a serum of a known positive control. Overlay with toluol and proceed as above.

In Thimble No. 3. Place 1 G placental peptone and 2 c.c. of a known negative serum or with the inactivated (heated to 60° C.) serum used in the test.

Serum control. A thimble containing only 2 c.c. serum.

TESTS FOR THE "CLEAVAGE PRODUCTS" OF ALBUMIN.

- (A) Biuret test.
- (B) Ninhydrin or Triketohydrinden Hydrate reaction. This is preferred to the Biuret test.

NINHYDRIN REACTION.

1. Remove 10 c.c. of the dialysate by means of a pipette dipping below the toluol and place this in a large test tube.
2. Add 0.2 c.c. of a watery solution of ninhydrin (1%).
3. Heat rapidly to boiling point and keep boiling 1 minute.

Positive reaction. A deep blue color appears immediately or after standing a short time.

Negative reaction. Either no coloration at all or perhaps a slight yellow.

Time of appearance. Reaction may be obtained in middle of the second month.

Reaction disappears in from 10 to 15 days after delivery.

BIURET TEST.

1. Remove 10 c.c. of the dialysate as in other method.
2. Add 5 c.c. of 33% sodium hydroxide solution and mix.
3. Titrate from a biuret with 0.25% copper solution drop by drop in such a manner as to form a "contact ring."

Positive reaction. Peptone yields a violet red to a pure red contact ring sharply differentiated from the lower colorless and upper blue solutions.

Negative reaction. Distinct bluish ring.

CHAPTER IV.

FORENSIC MEDICINE.

Tests for Blood.

INTRODUCTION.

In medico-legal cases, no tests for blood should be performed until the following points have been noted:

1. The exact time and exact part of the clothing or other object from which the specimen was taken.
2. If the blood is to be scraped from an instrument, describe fully.
3. Note shape and size and direction of all stains. (The small part of the spatter points to the opposite direction of the hemorrhage.
4. Specimens sent to you must have been properly sealed; the sender's name recorded; date and time of delivery noted, and seal must be unbroken.
5. Examine only a small portion of the specimen. Keep the remainder for corroborative evidence.

SPECIAL REMARKS.

1. Before giving an opinion, it is well to remember that blood cannot always be differentiated with **absolute certainty** from blood from other sources.
2. Blood appearing on one's person may be there accidentally by reason of one's occupation, e. g., butchers. Or, in women, menstrual blood must be considered.
3. Time not only alters the appearance of blood, but also influences the tests for blood.
4. Blood stains upon a knife or other metal must be distinguished from rust or lemon stains. All weapons should be examined immediately.
5. Blood stiffens all fabrics. Under a hand microscope, blood stains on linen give a dark crimson reflection, are glossy, smooth or reddish brown.
6. The action of various substances such as mortar, brick, lime, strong acids or alkalies, leather, chemicals in wall paper, starched clothing, etc., may so change the blood or impair its reactivity to certain tests so that no definite conclusions can be drawn.

1. Finding Red Cells in Dissolved Stains.

(Is the Surest Proof of Blood.)

COMPARATIVELY RECENT STAINS.

Are soluble in cold water.

The R. B. C. are, however, somewhat deformed but present the morphological characteristics described on p. 34.

Mammalian R. B. C. with few exceptions are circular and non-nucleated.

Oviparæ are ovoid in shape and show a central aggregation of granules resembling a nucleus.

Mammalian corpuscles are the smallest of all excepting the musk-deer (1/12,000 of an inch).

The corpuscles of reptiles are the largest.

The central granules above described can be made more distinct by adding acetic acid.

The corpuscles are small in elephants, pigeons and toads.

When a stain is dissolved in water, the color of the solution is found to vary with the age of the stain.

A **very recent** stain produces a bright red solution owing to the passing out of the Hb. from the R. B. C. into the water (hemolysis).

OLDER STAINS.

Hemoglobin is less soluble and methemoglobin is the result.

EXCEEDINGLY OLD STAINS.

Insoluble in water; soluble in dilute citric acid and in ammonia water.

A clot can be disintegrated by dissolving its albumin with a 33% solution of KOH or a 50% glycerine solution. The best examining fluid is **Marx's fluid**. It stains the R. B. C. red. It consists of:

Quinine hydrochlorate (1:1,000 sol.).....10 c.c.
Potassium hydrate (33% sol.).....10 c.c.
Eosin, q. s. to tint.

2. Julius von Kóssa's Test.

1. Take 10 c.c. of the watery solution to be tested.
2. Add 10 c.c. of 90% alcohol and 5 c.c. chloroform.
3. Mix gently but **DO NOT SHAKE**.

Positive reaction. The hemoglobin is dissolved and appears on top of the layer of chloroform as tiny red droplets.

For urine. Use 10 c.c. urine, 10 c.c. distilled water, 5 c.c. alcohol, 5 c.c. chloroform and mix gently.

3. Van Deen's Guaiac Test.

1. To any volume of the watery solution to be tested add an equal volume of freshly prepared guaiacum resin in alcohol.
2. By floating either (a) peroxide of hydrogen, (b) ozonized oil of turpentine, or (c) oil of eucalyptus a blue sapphire color is **immediately** formed at the point of contact and on shaking the color will spread throughout the mixture.
3. If the stain be very old, apply the chemicals direct on the fabric and immediately place a piece of filter paper on the spot and the latter will turn blue.

Note.—The blue color must occur **after** the peroxide is added. It is a good confirmatory test.

Test may not be obtained after stain is 2½ years old.

It is more reliable in its negative phase than when positive because many other substances give a positive reaction. They are:

Potassium permanganate.
Peroxide of lead.
Peroxide of manganese.
The halogen group.
Nitric and chromic acids.
Ferric chloride,
Copper salts.

Potassium ferro- and ferri-
cyanide.
Gum acacia.
Gluten.
Unboiled milk.
Raw potato pulp.
Pus.
Any living cell or its intra-
cellular enzymes.

4. Schaer's Test.

Technic. Similar to that of the guaiac test excepting that a 1 to 4% solution of aloin in alcohol is used instead of guaiac.

Positive reaction.

1. When the tincture of aloin is added to the suspected solution a red color appears, quickly assuming a cherry-red appearance when ozonized oil of turpentine is added.

2. The pink color should develop within a short time. There are substances which produce this coloration in a few hours.

Note.—The tincture should be freshly prepared because such color changes occur spontaneously of itself on standing.

5. Phenolphthalein Test.

1. To 1 part of the watery solution of blood to be tested add
2. Two parts of the following reagent prepared thus:
 - (a) Mix 1 c.c. of N/10 NaOH with a few c.c. distilled water, with a slight excess of phenolphthalein.
 - (b) Shake thoroughly and filter.
 - (c) To the filtrate add:

Sodium hydrate.....	20	c.c.
Peroxide hydrogen (3%).....	0.1	c.c.
And make up to.....	100	c.c.

Allow to stand a few minutes.

Note.—Fresh solutions are devoid of any pink coloration but will be so in time.

Positive reaction. A pink to a red color depending upon the amount of blood present. The test is so delicate that it will detect blood even in the proportion of one part blood to eight million of water.

Testing for blood in the secretions and excretions.

1. Extracts of various animal tissues or various secretions of the body interfere with the test so that blood cannot be recognized in such great dilutions as when watery solutions are employed.
2. Boiling these solutions prior to the test removes most of the objections. Or,
3. If the secretions be treated with a thick cream of aluminium hydrate suspension, the precipitate will carry down the blood pigment and thus concentrate it.

A small amount of this precipitate (whether derived from urine, feces suspension, exudates, etc.), will show a decided color when added to 2 c.c. of the reagent.

6. Teichmann's Hemin Crystals.

1. Place some dried blood on a slide and add a drop or two of glacial acetic acid. Cover with cover slip.
2. Two drops of common salt solution (2 grains to 8 ounces of water) are added in case the blood is very old.
3. Heat the slide gently so that the fluid steams but does not boil. As the acid evaporates, allow more to run under the cover slip.
4. After the slide cools mount in glycerine.

Positive reaction. Dark brown rhombic plates and prisms appear. Star-shaped clusters with rounded angles are also quite common. The crystals cross each other so as to resemble the letter "X."

The reaction may thus be expressed:

Hemoglobin + acetic acid + NaCl = globin + HCl + hematin;
Hematin + HCl = Hemin crystals (hydrochlorate of hematin).

Note.—If blood be mixed with iron rust, the hematin test will be negative.

7. Spectroscopic Absorption Bands.

Introduction. The various solutions of hemoglobin and its derivatives produce characteristic absorption bands which always occupy definite and constant positions with relation to the Fraunhofer's lines.

These lines are vertically placed and appear as dark slits. They are 8 in number and lettered from A to H.

Recent stains.

If on fabric, cut it in small strips and place into glass-stoppered vials (capacity of $\frac{1}{4}$ -ounce, but only $\frac{3}{4}$ full with distilled water).

When the solution becomes red or reddish brown remove some of it by means of a capillary pipette and insert it into the cell chamber of Zeiss's Microspectroscope and examine for absorption bands.

It is to be especially noted that bands are only visible when the solutions are of a certain strength and certain depth (depth of 1 cm. and strength of 0.85 to 0.65%).

Oxyhemoglobin.

In the above dilution and depth 2 bands are seen between the D and E positions.

The alpha band nearest D being narrower but darker than the beta band nearest E.

In weaker dilutions, the beta band disappears first.

With greater concentration, the two bands become broader and the space between them narrower and the blue and violet ends of the spectrum disappear.

By adding a particle of ferrous sulphate, a particle of Rochelle salt and a little ammonia, the two bands are reduced to one band. This is called **reduced hemoglobin** or **Stoke's band** (the ingredients given above forming Stoke's reagent).

Hemoglobin, also called **reduced hemoglobin**, is more soluble than oxyhemoglobin.

Its solutions are more violet or purplish than those of oxyhemoglobin of the same strength.

Hemoglobin solutions absorb the blue and violet rays to a less extent than those of oxyhemoglobin but they strongly absorb the rays lying between the C and D lines.

As before stated, with proper dilution, its spectrum is that of one broad band not clearly defined between D and E, lying towards the red end of the spectrum a little over the D line.

Old stains. Oxyhemoglobin having been converted into hematin which is insoluble in water, it becomes necessary to add a few drops of acetic acid and the bottle must be permitted to stand in a warm place for several hours.

Examine some of this solution for **acid hematin** bands. The bands can be reduced by Stoke's reagent.

ACID HEMATIN shows 4 bands:

1. Between C and D.
2. } Another broad band not clearly defined between D
3. } and F, which, under certain conditions divides into 2 narrower bands.
4. A fourth band between D and E, which is nearer D and very weak.

ALKALINE HEMATIN:

One band between C and D which reaches out to some extent between D and E.

If this alkaline solution be reduced with ammonium sulphide we obtain the spectrum of **hemochromogen**.

HEMOCHROMOGEN. Shows 2 bands:

1. Is very sharp and dark between D and E.
2. Paler and broader band covering the E line.

HEMATOPORPHYRIN.

Is isomeric with bilirubin and is formed when hematin is treated with concentrated sulphuric acid in the presence of air. It loses its iron constituent. It is insoluble in water.

In acid solution. Two bands.

1. A faint and narrow band between C and D but nearer D.
2. Another darker, sharper and broader band in the middle between D and E.

In dilute alkaline solution. Four bands.

1. One band between C and D.
2. A broad band covering D but its broadest portion between D and E.
3. Between D and E, nearly at E.
4. A fourth band, broad and dark between E and F.

Importance. Medico-legally very important because certain old stains can be identified only by its spectrum.

METHEMOGLOBIN.

In watery or slightly acid solution.

Its spectrum resembles that of acid hematin but with this difference: it easily is converted into hemoglobin by reduction with alkali. On the other hand, when acid hematin is reduced it is converted into hemochromogen.

In alkaline solution.

Its spectrum resembles that of oxyhemoglobin but with this difference: that the band nearest E is stronger than that at D. According to Hammersten a third band occurs between C and D.

Significance. Occurs in cases of poisoning with: potassium permanganate, potassium ferricyanide, chlorates, nitrites, nitrobenzol, acetanilide, antipyrin, turpentine, sulphonal, arsenic and in cases of cyanosis with diarrhea. Hemorrhagic transudates and cystic fluids due to spontaneous decomposition of blood.

CARBON MONOXIDE HEMOGLOBIN.

Two bands between the D and E lines but they are situated more to the left (violet end) of the spectrum. It cannot be reduced.

It is found after coal gas or illuminating gas inhalation and may even be demonstrated for a short time after death.

In severe but not fatal cases it may persist for several days.

8. The Precipitin Reaction.

NOTE.—This test is used medico-legally for the detection of blood and blood serum, but in reality it is a specific test for blood proteid and not for blood. Other tests must prove the presence of blood.

Soluble proteid may give this test at a period as late as 50 years. It is a very delicate test.

BASIS. The serum of an animal injected with blood or blood serum of another animal, shows the property, when added to an homologous serum, of precipitating the albumin of this serum in the form of a light flocculent precipitate. Of course, human serum is used in medico-legal cases.

TECHNIC.

1. Add a sufficient amount of NaCl to the dried blood to get it in solution. If the stain is upon clothing, cut the stain out, tease it and allow it to stand in salt solution one hour. (Old stain 24 hours).

2. Filter these solutions twice.

Once through hardened filter paper.

Then through a small Berkefeld filter.

3. Add a sufficient amount of salt solution to make approximately a 1:1,000 solution of the stain. This filtrate must be clear and neutralized by adding some tartaric acid or sodium carbonate solutions.
4. Take 10 test tubes of equal size and thickness. Label them from 1 up to 10. Fill as follows:

Tube No. 1. 1 c.c. of the above solution of the stain.

Tube No. 2. 1 c.c. of the above solution of the stain.

Tube No. 3. 1 c.c. of a 1:1,000 dilution of a known fresh human blood in normal salt solution.

- Tube No. 4. 1 c.c. of a 1:1,000 dried human blood in 0.9% salt solution.
- Tube No. 5. 1 c.c. sterile salt solution.
- Tube No. 6. }
- Tube No. 7. } 1 c.c. of 1:1,000 dilution of either fresh
- Tube No. 8. } or dried blood of such domestic ani-
- Tube No. 9. } mals as chicken, dog, horse, sheep.
- Tube No. 10. 1 c.c. of physiological salt extract of the matter upon which the stain was found.

To every tube except No. 2, allow 0.1 c.c. anti-serum (see below) to trickle down from a graduated pipette along the side of the tubes.

To tube No. 2, add 0.1 c.c. of normal clear rabbit serum.

Positive reaction. Within 2 minutes, tubes 1, 3 and 4 which contain human blood become turbid. The others do not contain blood, hence are clear. (Contact-ring turbidity.)

Preparation of Anti-Serum for the Precipitin Reaction.

This is the serum of the animal immunized against the proteids of a particular species of animal.

1. Inject a rabbit intraperitoneally with 5 to 10 c.c. of whole blood or serum.
2. Repeat said injections at intervals of 3 to 5 days until 6 or 8 injections have been made.
3. Allow one week to elapse after the last injection.
4. Obtain a few drops of blood by puncturing rabbit's ear and allow same to clot in a small test-tube and the serum which exudes is then tested for its potency.
 - (a) First make a 1:1,000 dilution of homologous blood in physiological salt (0.9% NaCl). Only 1 c.c. is necessary. Place in test tube. If the dilution has been properly made, a foamy layer forms on shaking and if 1 c.c. of this dilution is taken and to it 1 drop of a 25% nitric acid solution added a slight opalescence will occur.
 - (b) Add the anti-serum to the above dilution. If a turbidity appears within 1 to 2 minutes the serum is sufficiently potent for the test.
5. Bleed the animal. (Either partially or total exsanguination.)

- (a) Collect blood in wide-mouthed test tubes and plug with cotton. Allow to coagulate like agar slants.
- (b) Remove the exuded serum (which must be clear), place in test tubes, plug with cotton, seal with paraffin, store in refrigerator. This is the anti-serum.

DIFFERENTIATION OF BLOOD FROM IRON RUST.

Take some of the rust on the knife and place in a porcelain capsule containing HCl and heat gently.

If iron be present, the solution becomes yellow.

To potassium ferrocyanide add 1 drop of the yellow solution and the color turns blue.

To potassium sulphocyanide, add a drop of this yellow solution and a deep red color is the result.

DIFFERENTIATION OF BLOOD FROM RED PAINT.

The pigments in red paint are usually iron oxide and lead oxide.

Dried paint is insoluble in water but soluble in strong alkali solution or oil of turpentine.

Take some of this solution and allow to evaporate upon a watch glass.

Test for iron as previously described.

Lead is recognized by its vermilion color.

CHEMICAL TESTS for lead are:

1. The addition of potassium bichromate to any solution containing lead causes the precipitation of a yellow amorphous deposit, soluble in potassium hydroxide and strong HCl, but insoluble in acetic acid.
 2. Hydrogen sulphide passed through lead solutions results in the precipitation of black lead sulphide.
-

CHAPTER V.

OPSONINS.

DEFINITION.

Opsonins are certain substances probably belonging to the class of globulins, present in the blood serum which render the various forms of bacteria which invade the body subject to phagocytosis.

Phagocytosis signifies the power leucocytes have of incorporating in their bodies and destroying and digesting pathogenic bacteria. The leucocytes, therefore, play an important part in immunity.

Opsonins may be increased artificially by injecting certain **bacterial vaccines**.

Vaccines are suspensions in physiological salt solution of killed pathogenic bacteria. Vaccines produce an **active immunity**; that is to say, the patient himself is stimulated to produce his own antibodies.

Sera differ from vaccines in that serum already contains the antibodies formed in the body cells of the horse or other animal and are simply supplied to the patient. Thus, **passive immunity** is established. Sera begin to act shortly after injection while it takes a few days before vaccines begin to act. But, the immunity established by the use of vaccines lasts longer than in the other case.

The opsonins differ according to the various forms of bacteria present in the body. Thus, the varying degree of susceptibility of various persons to disease may be explained. Clinically, we find a decrease in the opsonins in certain bacterial infections.

Whenever a patient shows a decrease in the phagocytic power to any organism invading his body and we know these infecting germs, we can increase his phagocytic power by injecting him with dead cultures of these specific germs. (Vaccines.)

Autogenous vaccines are preferable to stock vaccines. By autogenous vaccines we mean vaccines made from the patient's own discharges. For therapeutic use they are better than stock vaccines. It is sure to contain all the germs responsible for the infection.

Opsonic Index. Expresses a comparison between the phagocytic power of the patient to that of a normal individual. The number of bacteria incorporated by the W. B. C. of such normal person is regarded as one.

Determination of Opsonic Index. Four things necessary:

1. Patient's serum.
2. Normal control serum.
3. Washed leucocytes.
4. Bacterial emulsions.

Technic.

1. Draw one volume of washed corpuscles into a capillary tube.
2. To it add a similar volume of patient's serum.
3. To this, add a similar volume of the specific bacterial emulsion.
4. Blow these 3 volumes into a dish and redraw up into the tube. (This insures proper mixing.)
5. Make another mixture like the above, excepting that the control serum is substituted for the patient's serum.
6. Incubate both for 15 minutes at 37° C.
7. Blow 1 drop on a glass slide, make a smear, fix and then stain with any of the polychrome dyes or with special bacterial stains.
8. Count about 100 polymorphonuclear leucocytes and note the number of germs incorporated within their protoplasm. By dividing this number by 100, we obtain the grand average for one leucocyte. This number represents the phagocytic index. To obtain the opsonic index, divide the patient's value just obtained by that of the control in paragraph 5 above.

Vaccines also used for Diagnostic Purposes.

- | | |
|---------------------------|---------------------|
| 1. Tuberculin test..... | } For tuberculosis. |
| 2. Moro's test..... | |
| 3. Von Pirquet..... | |
| 4. Calmette reaction..... | |
| 5. Luetin reaction..... | For syphilis. |

HEMATEMESIS—GASTRORRHAGIA.

DEFINITION.

A symptom denoting the appearance of blood in the ejected gastric contents.

ETIOLOGY.

1. GASTRIC CAUSES.

- | | | |
|-----------------------|---|---------------------------------------|
| (a) Ulcer of stomach | } | Usually chronic.
Multiple attacks. |
| (b) Ulcer of duodenum | | |
| (c) Cancer of stomach | } | Usually acute attacks. |
| (d) Corrosive poisons | | |
| (e) Trauma to stomach | | |

2. HEPATIC CAUSES.

- (a) Cirrhosis of liver, especially atrophic.
- (b) Passive congestion of liver.
- (c) Thrombosis of portal vein or compression of portal vein by a tumor.

3. SPLENIC CAUSES.

- (a) Enlargement, especially spleno-medullary leukemia.
- (b) Splenic anemia.

4. TOXIC CAUSES.

- (a) Yellow fever ("black vomit.")

5. HEMORRHAGIC DIATHESIS.

- (a) Hemophilia.
- (b) Scurvy.
- (c) Purpura.

SYMPTOMS AND DIAGNOSIS.

- 1. See under secondary (hemorrhagic) anemia, p. 6.
- 2. For differentiation between hematemesis and hemoptysis, see p. 104.
- 3. Tests for occult blood in gastric contents.

SPECIAL REMARKS:—

Atrophic cirrhosis of the liver.

Hematemesis occurs here as one of the so-called "obstructive symptoms."

In fact, hemorrhage may occur anywhere in the body.

The association of a small liver with ascites, gastrointestinal catarrh, hematemesis and hemorrhoids is very suspicious of atrophic cirrhosis.

Following hematemesis melæna may occur.

It is to be specially noted that hemorrhages from the bowel may occur for several years and yet there be no vomiting of blood.

An associated enlarged spleen further accounts for the hematemesis.

Hepatic congestion.

A congested liver is often depleted by an attack of hematemesis.

In fact, hepatic congestion most often results from chronic valvular disease and pulmonary affections. Hence such losses of blood are often attended by beneficial results. It relieves the embarrassment of the heart. The improvement is, however, only temporary.

A congested liver is enlarged and pulsating.

Spleno-medullary leukemia.

Hematemesis and epistaxis are the two most frequent forms of hemorrhage.

A profuse hemorrhage reduces the size of the spleen.

Though intestinal hemorrhage is uncommon a severe diarrhea will nevertheless reduce the size of the spleen.

Splenic anemia.

Hematemesis is very common and is also associated with splenomegaly.

The liver may subsequently be involved in a secondary cirrhosis which of itself causes further hemorrhage, ascites, jaundice, etc.

Malarial cachexia.

In malarial cachexia which follows repeated attacks of any of the malarial fevers, fatal attacks of hematemesis may occur.

The spleen is enormously enlarged. (Ague-cake spleen.)

DIFFERENTIAL DIAGNOSTIC TABLE.

	GASTRIC ULCER.	DUODENAL ULCER.	GASTRIC CANCER.
AGE AND SEX.....	Women, 67%. Puberty.	Males: 25 to 45 years.	Later in life. 75% occur between ages of 40 and 70.
DYSPEPTIC SYM-TOMS.....	Nausea and vomit. Vomiting occurs within first 2 hours after eating. Vomiting affords relief from pain.	May be totally absent. If vomit does occur it is never severe. Appetite very good.	Early, progressive and unremitting in severity. Vomiting usually delayed one hour or more after eating.
HEMATEMESIS	Hemorrhages usually profuse, especially if an artery be eroded. More apt to occur after eating. Usually multiple attacks. May sometimes be first symptom. Blood first appears in vomit, then in stools.	Very small amount of blood in vomit, if any at all. Blood first appears in stools, giving them a tarry color.	Never so profuse like in ulcer. Coffee-grounds vomit. Color is dark brown or black in contrast to bright red of ulcer. Blood is here altered but not so in ulcer.
PAIN	Induced by eating. Occurs $\frac{1}{2}$ half to 1 hour after eating. An early symptom in 80%. Occurs in paroxysms—aburning, boring or gnawing. Epigastric location. Radiation to back. Vomiting affords relief. Relieved by alkalies, anæsthene, and a diet of peptonized milk within one week.	2 to 4 hours or more after eating. "Hunger pains." Relieved by eating, but only temporarily. In right hypochondrium or in median line slightly above the navel. Distinct remissions periods when pain disappears. May be relieved by alkali.	Occurs early, never disappearing entirely. Usually epigastric. Continuous, seldom paroxysmal. Usually aggravated by food. Not relieved by vomiting. Does not radiate as often as in ulcer. Peptonized milk diet does not control pain.

DIFFERENTIAL DIAGNOSTIC TABLE—Continued.

	GASTRIC ULCER	DUODENAL ULCER	GASTRIC CANCER
LOCAL TENDERNESS	In epigastric angle. At Boas' point—to left of spine at level of 10th to 12th dorsal vertebrae.	At a point 2 inches above the umbilicus on a line drawn between the umbilicus and cartilage of 9th rib.	On pressure over epigastrium. Head's areas of skin tenderness in upper abdominal zone. Local tumor.
LOSS IN WEIGHT.....	Not as marked as in cancer. Slight anemia.	Physical condition usually very good.	Progressive emaciation and cachexia due to malignant nature. Marked anemia which may approach pernicious anemia type.
GASTRIC ANALYSIS..	Amount normal. Blood present. Marked hyperacidity.	High, free HCl and total acidity, with much incorporated mucus. Blood is rare.	Quantity increased. Blood present. Lactic acid abundant. HCl decreased or absent. Boas-Oppler bacilli, sarcinae, etc.
STRING TEST.....	Discoloration at 40 c.m. signifies ulcer at cardia. Between 44 and 54, lesser curvature. Between 56 and 58, pylorus.	59 cm. and over signifies ulcer in duodenum. Blood may also be microscopically evident in the bucket.	Salomon's test. Grafe's and Rohrer's hemolytic test. Neubauer and Fischer's Tryptophan test. Gluzinski's tests.

The hemorrhages and the parasites cause severe secondary anemia.

Retinal hemorrhages very common.

Yellow fever.

Black vomit occurs on third day during the rising course of the fever and a synchronous decline of the pulse rate—which is a peculiar combination. Hematemesis may reoccur during the secondary fever.

DIFFERENTIAL DIAGNOSIS.

HEMATEMESIS	HEMOPTYSIS.
1. Previous history points to gastric, hepatic or splenic disease.	1. Cough or signs of some pulmonary or cardiac disease precedes the hemorrhage.
2. The blood is brought up by vomiting, prior to which the patient may experience a feeling of giddiness or faintness.	2. The blood is coughed up and is usually preceded by a sensation of tickling in the throat. If vomiting occurs, it follows the coughing.
3. The blood is usually clotted, mixed with particles of food and has an acid reaction.	3. The blood is frothy, bright red in color, alkaline in reaction. If clotted, rarely in such large coagula and mucus may be mixed with it.
4. Subsequent to the attack the patient passes tarry stools and signs of disease of the abdominal viscera may be detected.	4. The cough persists, physical signs of local disease in the chest may be detected. The sputa may be blood-tinged for several days.

HEMOPTYSIS.

DEFINITION.

A symptom denoting coughing up of blood.

CAUSES.

1. PULMONARY.

(a) TUBERCULOSIS.

May occur at any stage of the disease.

In fact, a brisk hemorrhage may be the first symptom to lead us to examine the lungs. In these cases we will find pulmonary signs quite marked, although only one hemorrhage has occurred.

Repeated attacks usually occur at any time with or without cause.

The amount of blood lost varies from blood-tinged sputa to cup fulls.

It seems paradoxical to state that many tubercular patients stand these losses of blood well as evidenced by the temporary improvement in the dyspnea, chest oppression and cough. Repeated attacks, however, cause depression.

If the hemorrhage be followed by persistent rise in fever or by the appearance of fever where none has previously existed, it means that the destruction of lung tissue is going on rapidly.

A purulent sputum intimately admixed with blood is very frequent and is diagnostic of cavity formation.

(b) **PNEUMONIA.**

The usual history is that a blood-tinged sputum becomes manifest within 24 hours after the initial congestive chill.

In some cases a free hemorrhage may mark the onset of the disease.

The sputum is extremely viscid and tenacious.

The admixture of the blood and viscid mucus is called "prune-juice" expectoration.

Although R. B. C. may be found intact in the sputum, the largest proportion is found dissolved in the sputum thereby giving the sputum a "rusty" color.

In some cases a simple catarrhal exudate is found throughout the entire course of lobar pneumonia.

(c) **Abscess, gangrene, cancer and syphilis of lung.**

(d) **Pulmonary congestion** (including hypostatic congestion and pulmonary edema.

In these cases the sputa are watery and blood-tinged and seldom profuse.

2. **CARDIAC.** With failing compensation of the heart we find an increase in mechanical congestion of the lung. Expectoration then becomes decidedly blood-streaked.

Pulmonary engorgement occurs earlier in mitral than in aortic disease. In fact, it is seldom seen in aortic regurgitation.

3. ARTERIAL.

Thoracic aneurism. According to Osler, the bleeding may have its origin from:

- (a) Soft granulations in the trachea at point of compression, in which cases the sputa are blood-tinged.
- (b) Rupture of the aneurismal sac into the trachea or bronchi.
- (c) Perforation into lung or erosion of lung tissue.

The bleeding may be profuse, rapidly proving fatal and is a common cause of death.

It may persist for weeks or months, in which cases it is a hemorrhagic weeping through the sac which is exposed in the trachea.

Death from hemorrhage is relatively more common in aneurism of the third portion of the arch and of the descending aorta.

According to Broadbent, the aneurism of "physical signs" springs from the ascending aorta while the aneurism of "symptoms" springs from the transverse arch.

4. Rarer causes.

- (a) Ulcerative affections of larynx, trachea or bronchi.
- (b) Vicarious menstruation.
- (c) Gout.
- (d) Purpura hemorrhagica.

HEMATURIA.

DEFINITION.

Blood in the urine. It is a symptom and not a disease.

CAUSES.

1. RENAL.

- (a) Stone in kidney.
- (b) Tuberculosis.
- (c) Tumors.
- (d) Inflammations.

Acute Bright's.

Acute exacerbations of chronic Bright's.

Septic nephritis.

- (e) Congestion.
- (f) Chemicals: turpentine, carbolic, cantharides, etc.
- (g) Infarction as in septic endocarditis.
- (h) Injury to loins.
- (i) Parasites.

Filaria sanguinis hominis.

Bilharzia.

2. URETERAL CAUSES.

- (a) During passage of stone in ureter.

3. VESICAL CAUSES.

- (a) Stone in bladder.
- (b) Tumors.
- (c) Ulcer of mucosa: usually tubercular.
- (d) Hemorrhagic cystitis.

4. URETHRAL CAUSES.

- (a) Gonorrhea.
- (b) Dilatation of stricture and meatotomy.
- (c) False passage with instrument.
- (d) Stone.
- (e) Papilloma and urethral caruncle.
- (f) Fracture of pelvis.
- (g) Ulceration and fissure at bladder neck.

5. PROSTATIC CAUSES.

- (a) Enlarged prostate.
- (b) Hard small fibrous prostate with erosion of bladder mucus membrane.

6. INFECTIOUS FEVERS. Especially scarlatina.

7. MALARIA.

8. LEUKEMIA.

LOCALIZING THE SOURCE OF THE HEMATURIA.

Only by direct examination with the urethroscope and the cystoscope and by ureteral catheterization can we localize the source of bleeding with absolute certainty.

SPECIAL REMARKS ON INDIVIDUAL DISEASES.

Tuberculosis of the kidney.

Hematuria appears at irregular intervals without assignable cause. It is never profuse.

Color of urine is milky white due to presence of pus. A sterile urine with a lot of pus. Urine is acid and contains tubercle bacilli.

Increased frequency of urination both day and night even before implication of bladder. Polyuria.

Renal tuberculosis is at first a unilateral disease.

Bladder always becomes secondarily involved. Cystoscopy reveals ulcerations usually around the vesico-urethral orifices and trigone and the ureteral openings. Congestions of the ureteral papillæ are typical and show ulcerations and hemorrhages.

Symptoms of cystitis soon develop.

Acute Bright's Disease.

Free blood in the urine gives the urine a "smoky" color.

Marked reduction in urinary output.

Associated with the blood we find various forms of casts: blood, hyaline, granular and epithelial.

Anemia and dropsy are associated characteristic features.

Passive congestion of the kidney.

Hematuria appears for a prolonged period; is seldom large in amount and usually associated with some diminution in urinary output.

Malignant disease of the kidney.

Hematuria appears and disappears suddenly without any assignable cause.

Bleeding persists in spite of any treatment.

It occurs as an early manifestation of the disease.

Renal calculus.

While bleeding usually occurs at the time when the stone migrates it may occur at any time.

During the attack of colic, excruciating pains are felt in the loin and extend into the testicle and to inner side of the thigh. After the attack a smoky urine is voided.

During the intervals between the attack both pus and blood will appear if the kidney has become involved in a suppurative inflammation.

Vesical Calculus.

Hematuria is an intermittent and not a constant and is almost invariably small in amount.

A few drops may be squeezed out at the end of urination or the blood may be mixed with the urine.

The associated symptoms are day frequency, pains which are referred to the glans penis, stoppage of the urine while in full stream and inflammation of the bladder (cystitis).

TESTS FOR BLOOD IN THE URINE.

1. **Microscopical.** Centrifuge the urine and examine a portion of the sediment for small circular discs which are more regular in form than any of the other morphological elements of the urine. They are non-granular and non-nucleated and smallest of the formed elements.

2. **Guaiaec test.**

Stratify some urine upon an equal mixture of ozonized oil of turpentine and a 1% alcoholic tincture of guaiacum.

A bluish ring appears at the junction of these liquids if blood be present.

Pus also gives a positive reaction but the ring disappears on boiling.

All urine before testing must be acid. If not, make it so by adding acetic acid.

3. **Julius Von Kóssa's Test.** (See p. 89.)

Sometimes, instead of tiny red hemoglobin droplets a rose-colored ring appears above the surface of the chloroform. In such cases, decant the supernatant liquid and add a few more c.c. of alcohol and then the red droplets will appear.

HEMATURIA MUST BE DISTINGUISHED FROM HEMOGLOBINURIA.

In hematuria R. B. C. are found but not in hemoglobinuria. Each has a specific absorption spectrum.

HEMORRHAGE INTO THE BRAIN.

MENINGEAL OR PIAL HEMORRHAGE.

Most frequent causes are fracture of the skull (usually over the anterior inferior angle of the parietal bones) involving the middle meningeal artery, and secondly rupture of miliary aneurisms.

The blood may be extra- or intradural.

In the latter instance, the blood finds its way into the subarachnoid space, therefore lumbar puncture should yield a bloody fluid.

Typical diagnostic symptoms are absent though they may, to some extent resemble those of intracranial hemorrhage. The symptoms depend upon the size and location of the hemorrhage.

Paralyses are usually absent.

Meningeal hemorrhage is the cause of 50% of all still-births. This may usually be explained by prolonged labors, instrumental delivery, etc.

In those cases where the child survives, idiocy may subsequently manifest itself.

INTRACEREBRAL HEMORRHAGE.

Hemorrhage takes place into the brain substance.

The most frequent location is in the neighborhood of the Circle of Willis at the base of the brain. The lenticulo-striate artery suffers most.

The cortical vessels are not as often affected as the central arteries.

These hemorrhages are of the concealed variety and although small in amount is attended by grave symptoms because the cranial cavity is compromised and pressure increased.

The symptoms of a "stroke" are given in the differential diagnostic table on page 112.

The abrupt onset is due to sudden compression of the brain.

The paralysis is due to the destruction of the motor area or any part of the pyramidal tract.

Only the lower part of the face is involved as compared to the entire side of the face in Bell's palsy.

The face is involved on the same side as the arm and the leg owing to the decussation of the upper motor segment of the facial nerve. The arm is more paralyzed than the leg.

Crossed paralysis means that the lesion is in the crus, pons or medulla, i. e., there is a paralysis of a cerebral nerve on one side with a loss of power (or sensation) on the other side.

When hemianesthesia is marked the lesion is usually in the internal capsule (posterior limb).

Emboli in cases of ulcerative endocarditis usually enter the left carotid artery and then carried to the cerebral arteries so that certain focal symptoms may occur:

Left middle cerebral artery; hemiplegia with aphasia.

Vertebral artery: acute bulbar paralysis.

Basilar: double hemiplegia with bulbar symptoms because of its relation to the pons.

Posterior cerebral: hemianopia and sensory aphasia.

DIFFERENTIAL DIAGNOSTIC TABLE.

	CEREBRAL HEMORRHAGE (Apoplexy)	CEREBRAL SOFTENING (Embolism)	CEREBRAL THROMBOSIS
AGE	Past 50.	Young persons: due to rheumatic endocardi- tis.	Both in young and old. Young: Syphilis.
HISTORY	Signs of arteriosclerosis, contracted kidney, cardiac hypertrophy.	Heart Disease: espe- cially endocarditis.	Old: Arteriosclerosis, cardiac hypertrophy, interstitial nephritis.
ONSET	Usually abrupt with coma.	Usually sudden coma of short duration.	Slow and prolonged; coma slight or absent.
PULSE	Slow and full.	Rapid and compressible.	Pulse is not full.
BLOOD PRESSURE...	Increased.	Lowered.	
RESPIRATION	Stertorous, deep, noisy.	Not stertorous; not so deep.	Respiration is not ster- torous.
FACE	Ashen gray or cyanotic.	Pallor (?) not always present.	Pale.
PUPILS	Dilated and unequal. Do not react to light. Conjugate deviation of eyes.		Syphilitic ocular signs are: Irregular, non circular pupils re- sponding sluggishly to light; ocular muscle paralyses.

DIFFERENTIAL DIAGNOSTIC TABLE—Continued.

	CEREBRAL HEMORRHAGE	CEREBRAL SOFTENING	CEREBRAL THROMBOSIS
TEMPERATURE	Normal or subnormal during coma.	Normal or a little above. The larger the embolus the higher the fever.	100° F.
REFLEXES	Absent during coma.		
HEMIPLEGIA	Face, arm and leg of same side are paralyzed except in lesions of lower part of pons, crus, and medulla. Paralysis appears immediately.		Approaches gradually, preceded by numbness and tingling. In the young there are multiple attacks, each time involving another part of the body.
ELECTRICAL RESPONSE.....	In all cerebral lesions there is no departure from the normal. The paralysis is flaccid and not accompanied by wasting.	Same.	Same.
APHASIA	Absent.	Present. Because left middle cerebral artery is usually affected.	Present. Besides loss of memory there is impaired speech, headache, dizziness and vertigo and stupor.
SECONDARY SYMPTOMS.....	Spastic Paraplegia. Exaggerated Reflexes. Febrile Reaction. Contractures.	Same.	Present; But when due to syphilis, recovery is complete because blood vessels are not entirely occluded.

UTERINE HEMORRHAGE.

Menorrhagia and Metrorrhagia.

DEFINITION.

Bleeding from the womb may occur either at the normal menstrual period or at any time between the menses.

Menorrhagia. Excessive menstrual bleeding.

Metrorrhagia. Bleeding between periods.

CAUSES. A majority of the cases occur in connection with labor and abortion.

1. Abortion and miscarriage. (Retained secundines; placental tissue.)
2. Subinvolution of uterus, the result of post-abortive or puerperal infection.
3. Chronic endometritis. (Fungosities.)
4. Backward displacement of the womb.
5. Uterine tumors.
 - (a) Polypi.
 - (b) Fibroid (only when endometrium is involved).
 - (c) Cancer.
6. Ovarian and tubal disease.
7. Impeded circulation as a result of cardiac, pulmonary or hepatic disease.
8. Menopause. (Suspicious of cancer.)
9. Postpartum hemorrhage.
10. Lacerations of cervix, vagina or perineum.
11. Placenta previa.
12. Ectopic pregnancy. (Concealed hemorrhage.)
13. Inversion of the uterus.
14. Tuberculosis and syphilis of the uterus.

SPECIAL REMARKS.

Menstruation.

1. A periodic phenomenon occurring monthly beginning in girls at about the 13th year.
2. Each girl soon develops a certain "standard." That is to say, that she flows a certain number of days, uses

a certain number of napkins and has a certain amount of pain, etc. Any deviation later in life from this standard means some abnormality.

3. The flow is most abundant at the onset. It is variously estimated from 2 to 8 ounces.
4. The average duration of the menstrual flow is 4 days.
5. Menstrual blood is dark in color, alkaline in reaction, not coagulable due to presence of mucus and contains epithelial cells. Prior to the appearance of the flow and for a few days after the flow has stopped, mucus is very abundant.
6. **Dysmenorrhea.** Excessive pains during menstruation.
7. The most frequent causes of prolonged menstruation are: polypoid endometritis, retroversion, subinvolution and uterine tumors.

ABORTION AND MISCARRIAGE.

THREATENED ABORTION.	INEVITABLE.	INCOMPLETE.	COMPLETE.
Hæmorrhage. Slight and usually free from clots.	Profuse, continuous, clotted, dark color.	Persistent; at times profuse, at others scanty, dark-colored and offensive.	Entire cessation of bleeding.
Pain. Not marked.	Cramp-like and severe.	Occasional attacks of pain.	Complete cessation of pain.
Cervical os. Slightly patulous.	Dilated.	Dilated and admits finger which feels portions of decidua membranes and blood clot.	Os retracted.
Uterus. Soft, enlarged. Angle of ante flexion between upper and lower uterine segments present.	Soft and enlarged, but this angle is effaced.	Large, soft and boggy, not involuting.	Large but retracted and firm; involution proceeding normally.
Discharge. Bright red blood color.	Dark blood, clots and portions of ovum.	Portions of ovum only.	Normal lochia which gradually ceases.

Chronic Endometritis.

In consequence to a long-standing congestion from whatever cause, the lining membrane of the womb is stimulated to excessive activity with the formation of **polypi or fungosities**.

These fungosities are directly responsible for the large amount of blood lost and for the prolongation of the menstrual period.

This chronic engorgement further incites connective tissue hypertrophy in the uterine musculature, with the result that the uterus becomes enlarged.

The other symptoms of this condition are obscured by the underlying pathological cause (which may be displacements, fibroids, lacerations of cervix, gonorrhea, etc.).

Retroversion of Uterus.

Chronic congestion of the womb resulting from backward displacement of this organ results in menorrhagia and dysmenorrhea.

The other diagnostic symptoms are: tenesmus, painful defecation, intermenstrual pain due to prolapse of the ovaries.

By bimanual palpation, the cervix will be found low down and anteriorly placed. The fundus cannot be palpated through the abdomen.

Uterine Fibroids.

Hemorrhage occurs only when the tumor involves the endometrium.

Hemorrhage is therefore profuse in cases of submucous fibroids. The usual term applied to these fibroids is "polypi."

Polypi tend to increase the surface area of the endometrium thus creating a larger bleeding surface.

In addition to menorrhagia we have metrorrhagia which is quite pronounced.

Interstitial or intramural fibroids also cause metrorrhagia but the subperitoneal variety does not.

When these polypoid masses obstruct the cervical canal we will find symptoms of obstructive dysmenorrhea and intermenstrual pain.

Uterine Cancer.

Irregular, atypical bleedings at the climacteric are suspicious symptoms.

Pain and foul discharge are late symptoms.

A lacerated, indurated and eroded cervix which bleeds easily when touched and is firmly attached to the underlying structures is very suspicious of malignant disease.

Post-Partum Hemorrhage.

1. While bleeding after delivery may come from the cervix, perineum or vagina, we restrict the usage of this term to hemorrhage from the **placental site**.
2. Post-partum hemorrhages usually occur within the first 24 hours after delivery.
3. The hemorrhage may be visible or invisible. When invisible the blood collects within the womb greatly distending it (hematoma).
4. The uterus is soft and flabby. A strongly contracted uterus is positive evidence against post-partum hemorrhage.
5. Predisposing causes are: protracted labors, injudicious use of anesthetics, hurried deliveries with or without use of pituitrin or instruments. Also hurried deliveries of the placenta.

EPISTAXIS.

DEFINITION.

Bleeding from the nose.

LOCAL CAUSES.

1. TRAUMATISM.

- (a) Blows on the nose.
- (b) Picking the nose causes the erosion of a thin-walled blood vessel on the cartilage of the septum just within the anterior nares about $\frac{3}{4}$ of an inch above the floor of the nose.
- (c) Indirectly in fracture of the base of the skull.
- (d) Operations on nose.

2. SPECIFIC ULCERATIONS.

- (a) Syphilitic.
- (b) Tubercular.
- (c) Malignant.

3. ANGIOMATA. (Bleeding polypi on septum.)

4. **ADENOIDS.** Children who have adenoids are subject to epistaxis and repeated attacks of "cold in the head."

By making a digital examination of the nasopharynx, the finger, when withdrawn, will be coated with a thick white-of-egg-like mucus and blood.

5. **FOREIGN BODY IN NOSE.**

The presence of a one-sided hemorrhage associated with a muco-purulent discharge in a child is suspicious of the presence of a foreign body in the child's nose.

CONSTITUTIONAL CAUSES.

1. As a diagnostic prodrome of typhoid.
2. In many conditions associated with an increased pulse tension as in cardiac, vascular and renal diseases. In the aged it is often a precursor of cerebral hemorrhage.
3. Hemophilia, scurvy and purpura.
4. Vicarious menstruation.

MELÆNA—ENTERRHAGIA.

DEFINITION.

Bloody stools or hemorrhage from the bowels.

ETIOLOGY.

1. **Diseases of the rectum.**
 - (a) Hemorrhoids. (Internal and external.)
 - (b) Anal fissure.
 - (c) Cancer.
 - (d) Fistulo-in-ano.
2. Gastric and duodenal ulcer.
3. Atrophic cirrhosis of liver.
4. Intussusception.
5. **Ulcerations of the bowel.**
 - (a) Syphilis.
 - (b) Typhoid.
 - (c) Cancer.
 - (d) Dysentery.
 - (e) Tuberculosis.
 - (f) Ischio-rectal abscess breaking through the bowel.
6. Severe enteritis. (Very rare.)

DIAGNOSIS.

It is very apparent that from the above enumerated causes that blood appearing at the anal orifice may originate from any portion of the gastro-intestinal tract.

As a general rule, it may be stated, that when the bleeding is high up, as for instance in the stomach and in the duodenum, the blood is never bright red in color but a black, tarry or coffee color. The black color is due to ferrous sulphide.

If the blood be adherent to scybalous masses or to well formed feces, it is usually derived from the rectum or anus and indicates piles.

If it be evenly distributed with the food material and brown in color, it indicates hemorrhage in the stomach or high up in the smaller bowels, especially if the stool be solid.

If evenly mixed with liquid stools the colon is usually the site of the bleeding.

It is useless to search for red cells in the feces except in cases of profuse hemorrhage.

The chemical tests for occult blood are: guaiac test, Weber's test, Adler's benzidin test, etc.

SPECIAL REMARKS.

Constipation is a great predisposing cause in the development of piles and at the same time, the passage of hardened feces over these blood tumors is very apt to favor rupture thereof, especially when straining. Consequently bleeding results. Repeated hemorrhages may result in severe secondary anemia.

In **atrophic cirrhosis** we find a diagnostic combination of bowel hemorrhages and hemorrhoids in consequence of the existing portal congestion. It is especially so in topers. In these cases, intestinal hemorrhages usually follow attacks of hematemesis. But, hemorrhages from the bowels may occur for several years without hematemesis.

In **intussusception** blood may appear in the stools spontaneously or after an enema has been administered. It is usually mixed with mucous. In children, the existence of a bloody and mucous diarrhea associated with a palpable abdominal tumefaction and severe tenesmus is very diagnostic of telescoping of the bowel.

A free intestinal hemorrhage may occur as a complication in **typhoid fever**. It seems strange that such hemorrhages may not be attended by bad effects. Usually occurs during the second or third weeks. It may be suspected if there be a progressive decline in the fever or in blood pressure. It usually comes on suddenly. Fatal collapse may sometimes supervene before the blood appears in the evacuations. In some cases, a slight hemorrhage may antecede a fatal hemorrhage. The bleeding arises from the sloughing ulcers on Payer's patches.

In both forms of **dysentery** we find a history of bloody stools at one time or other. Usually the stools are watery and blood streaked, but a pure bloody stool may also occur. Mucous may appear before the blood. Tenesmus is very characteristic.

Pus in association with blood in the stools usually signifies ulcerations in the bowels but it is not very excessive. When considerable pus appears in the stools it usually signifies that a neighboring abscess has ruptured into the bowels.

Cancer of the rectum and malignant disease of the bowels are invariably accompanied by pus and blood in the bowels.

GUAIAIC TEST for blood in the feces.

1. Rub up a small portion of the stools with water and then place same in a test tube.
2. Add glacial acetic acid ($\frac{1}{2}$ of the above volume).
3. Shake vigorously and add a few c.c. of ether.
4. Shake thoroughly again and allow to settle. (If blood be present, the ether takes on a brownish color. And, if the ethereal extract be not clear, add a few drops of alcohol.)
5. Stratify upon this ethereal extract a mixture of equal parts of fresh tincture guaiacum and ozonized oil of turpentine and a blue contact ring appears.

Note.—This is a good negative test. Meat must be excluded from the diet.

WEBER'S TEST for blood in feces.

1. A small portion of the stool is extracted with ether in order to remove the fat. Then it is separated from the ethereal solution.

2. Rub up this fat-free feces with water and proceed as in the guaiac test as stated under statements 2 and 3.
3. The ether takes up the hematin which can be detected by its absorption bands with the spectroscope.
 - (a) An intense narrow band in the red between C and D.
 - (b) A group of three broader bands:
 - (x) One in the yellow.
 - (y) One in the boundary line between the yellow and the green.
 - (z) One at the boundary between the green and the blue. This one is difficult to recognize.

Note.—A very reliable and sensitive test.

In order to avoid any confusion with the spectrum given by methemoglobin or by chlorophyll add alcoholic potassium hydrate, water and ammonium sulphide solution which reduces hematin to hemochromogen. This gives two bands in the green.

ADLER'S BENZIDINE TEST.

1. Extract the stool with a mixture of alcohol and ether.
2. Treat with glacial acetic acid. ($\frac{1}{3}$ of its volume.)
3. Shake thoroughly, allow to settle. If blood be present the ether becomes brownish in color.
4. This acid ethereal extract, which now contains the hematin, is treated with 2 c.c. of a saturated alcoholic benzidine solution and 2 c.c. of 3% peroxide of hydrogen.

In the presence of blood an intense green color appears.

It will recognize blood in the proportion of one part blood to 100,000 parts water.

It is chiefly valuable as a negative test.

Hemoglobin must be removed from diet. The same can be said about prunes.

ECTHOL.

A vegetable product; each teaspoon containing:

Thuja Occidentalis 3 grains
Echinacea Angustifolia.....28 grains

Local Action. An astringent antiseptic.

Indicated in inflammations of the skin, especially purulent inflammations like boils, carbuncles, abscess, erysipelas, mammitis, chancroid, ulcers and infected cuts.

It should be applied undiluted for topical applications. All collections of pus must first be incised and then washed with Ecthol.

It is not an antiseptic in the ordinary sense of the word but by its direct action upon the cells it stimulates them to overcome bacterial growth and aids in promoting healing. It is not poisonous like many other antiseptics.

Internal or Systemic Action.

In many diseases due to infection with pathogenic bacteria, especially the pyogenic variety, Ecthol, which consists of two vegetable products, heretofore regarded as alteratives, apparently stimulates the body cells to greater activity so that more **opsonins** are poured out into the blood, thus endeavoring to overcome the effects of the invading germs.

It may therefore be used in many blood disorders as a systemic antiseptic and a resistance promotor. It is recommended for internal use in acne, furuncle, carbuncle, erysipelas, pyelitis and especially septicemia.

Echinacea is also credited with being a febrifuge. Ecthol may therefore be also used in febrile conditions.

Dose.—One teaspoon 3 or 4 times a day.

BATTLE & CO.,
ST. LOUIS, MO.



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